OPTIC NERVE SHEATH DIAMETER (ONSD) MEASUREMENTS IN NORMAL SUBJECTS AND PATIENTS UNDERGOING CRANIOPLASTY AFTER DECOMPRESSIVE CRANIECTOMY FOR TRAUMATIC BRAIN INJURY –A PROSPECTIVE OBSERVATIONAL COHORT STUDY

Dissertation submitted to the Dr.M.G.R. Medical University, Chennai, for the M.Ch. Neurosurgery (6 years) Examination, August 2017

CERTIFICATE

This is to certify that the dissertation titled **"Optic nerve sheath diameter (ONSD) measurements in normal subjects and patients undergoing cranioplasty after decompressive craniectomy for traumatic brain injury – A prospective observational cohort study**" is bonafide original work done by Dr Akarsh J, submitted in partial fulfillment of the rules and regulations, for M.Ch. Neurosurgery (6 years) examination of the Tamil Nadu Dr. M.G.R. Medical University to be held in August, 2017.

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DECLARATION

This is to declare that this dissertation titled **"Optic nerve sheath diameter (ONSD) measurements in normal subjects and patients undergoing cranioplasty after decompressive craniectomy for traumatic brain injury – A prospective observational cohort study**" is bonafide original work done by me, submitted in partial fulfillment of the rules and regulations, for M.Ch. Neurosurgery (6 years) examination of the Tamil Nadu Dr. M.G.R. Medical University to be held in August, 2017.

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TABLE OF CONTENTS

AIMS OF THE STUDY

1) To evaluate and compare the change in measurements of optic nerve sheath diameter (ONSD) between Trendelenburg position (30 degree head down), supine and reverse Trendelenburg position (30 degree head elevation) in normal subjects.

2) To evaluate and compare the change in measurements of optic nerve sheath diameter (ONSD) between Trendelenburg position (30 degree head down), supine and reverse Trendelenburg position (30 degree head elevation) in patients before and after cranioplasty.

3) To attempt to correlate the changes in ONSD pre- and post-operatively with clinical outcomes.

INTRODUCTION

Patients who have large cranial defects following decompressive craniectomy undergo cranioplasty to cover the cranial defect for the protection of the brain from further injury as well as for cosmesis. In the presence of a large cranial defect, the intracranial pressure (ICP) can be influenced by atmospheric pressure. This is apparent as clinical deterioration in the upright position associated with a concomitant increase in intracranial pressure (ICP), producing motor as well as non-motor symptoms like neuropsychiatric disturbances, vague headache and generalized tiredness in patients with large skull defects. While reversibility of a motor deficit with a change in posture may be easy to document preoperatively before cranioplasty, the role of cranioplasty in reversing non-motor symptoms cannot be easily predicted. Optic nerve sheath diameter (ONSD) has been found to change with changes in intracranial pressure and hence an elevated ONSD may be used as a surrogate indicator of raised intracranial pressure (ICP).Measurement of ONSD could be useful in this subgroup of patients who have non motor symptoms in counseling them regarding whether cranioplasty may benefit them or not. With this background, we aim to measure ONSD using orbital ultrasound in patients admitted for cranioplasty following decompressive craniectomy for traumatic brain injury and study if a variation in ONSD can be detected with changes in posture. If we can detect an increase in the ONSD with raising the head end (indicating an increase in the ICP) we will attempt to correlate this with the degree of improvement in the postoperative period. We will also measure the ONSD in these patients in the three different positions in following the surgery to see if the degree of change in ONSD is decreased following the cranioplasty.

LITERATURE REVIEW

Anatomy of the optic nerve

The optic nerve is formed of 1.2 million axons from the ganglion cells in the inner most layer of the retina which converge at the optic disc. The optic disc is an area located slightly medial to the posterior pole of the eye ball. The optic nerve head is the proximal most area of the optic nerve where all axons from the retina converge. These axons are myelinated by oligodendrocytes at this region to form a 4 mm thick optic nerve. The central retinal artery and vein traverses through the initial part of the optic nerve till they exit the nerve 3 mm behind the globe.

The optic nerve is unique from other cranial nerves in that it is a direct continuation of cerebral white matter which is surrounded by subarachnoid space containing cerebrospinal fluid (1). Optic nerve is 5 cm long and 4 mm in diameter and is divided into four parts. The part of the nerve inside the globe is called optic nerve head or the intraocular part and it measures 1 mm. The axons from the ganglion cells acquire myelination at this part and form the optic nerve proper. The part inside the orbit is called intraorbital part and it measures 25 mm. The nerve then enters the optic canal for 9 mm and is called intercanalicular part. This part continues as the intracranial part which measures 12-16 mm long. In our study, the intraorbital part of the nerve along with dural covering this part of the nerve will be of main interest.

The optic nerve head consists of a surface nerve fiber layer, prelaminar region, lamina cribrosa and the retrolaminar region. The surface nerve fiber layers form the anterior most part of the optic nerve head. This nerve fiber layer is separated from the vitreous material by a membrane called the limiting membrane of Elshnig. The prelaminar layer lies posterior to the nerve fiber layer and is also called the choroidal part of the lamina cribrosa. This layer is the most important part of the optic nerve head where all pathological changes occur during raised intracranial pressure. After this layer comes the lamina cribrosa layer which is a thick network of connective tissue through which nerve fibers pass. The retrolaminar part of optic nerve extends from the ocular bulb till the nerve forms outside the globe. Myelination occurs in the retrolaminar part of the optic nerve head.

The area where the optic nerve leaves the eye ball is called optic disc. The optic disc is located 15 degrees nasal to the fovea. The fovea is optical focus center of the retina which has the maximum number of rods and cones. The optic disc area has no retinal photoreceptor cells and is represented on the visual field as the “blind spot”. The optic disc has a central depression called the optic cup which occupies the one third size of the disc.

Raised intracranial pressure and optic disc changes

Optic disc edema also called papilledema was first coined by Parson in 1908. This phenomenon refers to swelling of the optic nerve fiber layer in the optic nerve head due to axoplasmic flow stasis caused by increased intracranial pressure. The raised intracranial pressure is transmitted to the optic nerve sheath resulting in increased pressure in the CSF in the optic nerve sheath. This in turn causes pressure effects on the optic nerve resulting in axoplasmic flow stasis. The axoplasmic flow stasis results in swelling of the optic nerve fibers. The swelling of the optic nerve fiber layers also causes venous obstruction in the venules

inside the optic nerve resulting in back pressure changes and accumulation of extracellular fluid in the optic disc region. Thus the swollen optic nerve fibers along with extracellular collection of fluid leads to edema of the optic nerve disc. Optic disc edema usually develops 1-5 days after the onset of raised intracranial pressure.(2)

Optic nerve sheath

The intracranial subarachnoid space is in continuity with the subarachnoid space surrounding the intraorbital part of the optic nerve. The CSF space surrounding the optic nerve in its orbital course is surrounded by duramater which in turn is covered by periorbital fat. The duramater and arachnoid covering the intraorbital course of the optic nerve is referred to as the optic nerve sheath (ONS).

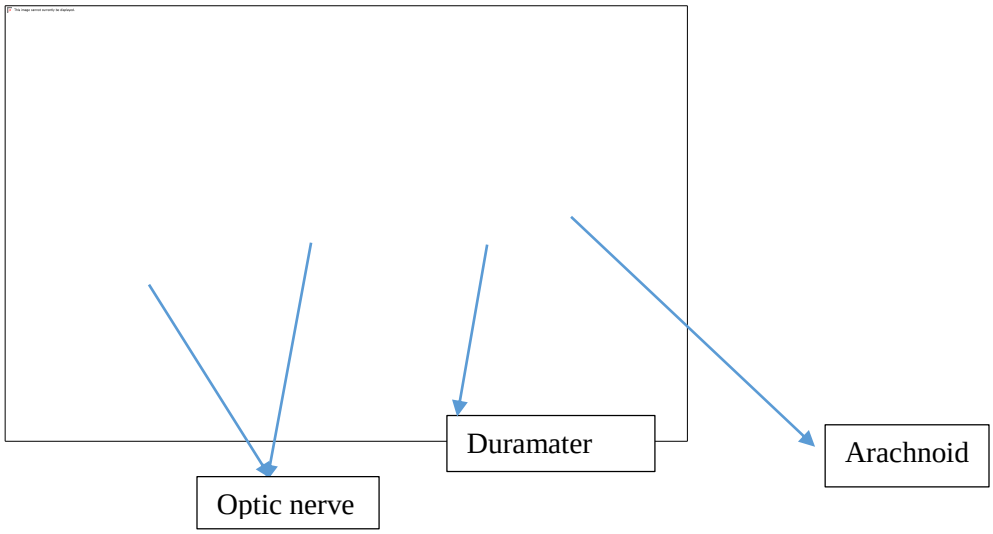


Figure 1 showing optic nerve sheath and subarachnoid space communicating with intracranial subarachnoid space

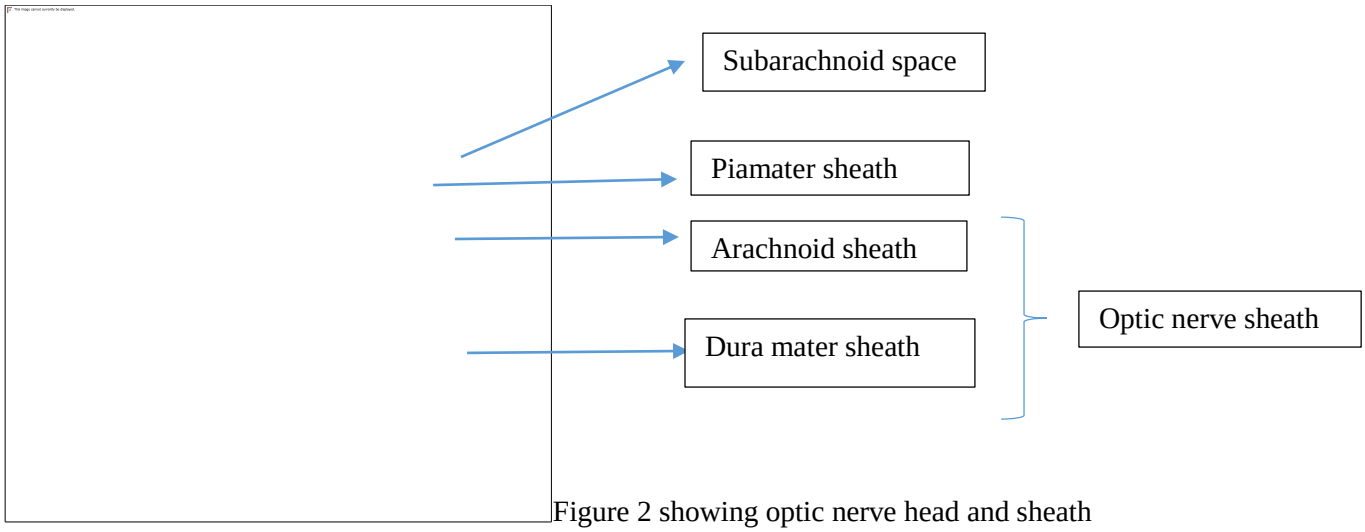


Figure 2 showing optic nerve head and sheath

Anatomically the optic nerve along with optic nerve sheath consists of a bulbar segment, mid-orbital segment and intercanalicular portion. (3) The widest part of the optic nerve surrounded by subarachnoid space and nerve sheath is just posterior to the ocular globe and is called the bulbar segment. This part of optic nerve has a unique anatomy compared to other parts of the optic nerve. It has been shown that the optic nerve sheath (ONS) in this area can be distended and collapsed by movement of CSF in and out of it. (4) This distension is more marked in the anterior segment of the intraorbital course due to the arrangement of the arachnoid trabeculations.

Various studies show that there is an obvious dilatation of CSF space in the bulbar segment of the optic nerve sheath called ampulla. This part of optic nerve sheath has multiple fined branched trabeculations in the subarachnoid space. The trabeculations form a delicate network and there are lamellae of fine flattened cells between each trabecula. The larger trabeculae may contain one or two blood vessels inside them. These trabeculations are covered with leptomeningeal cells which project into the subarachnoid space. The other two portions of the optic nerve sheath namely mid-orbital and the intercanalicular part of the nerve

sheath have numerous broad sepatations along with pillar-like structures which divide the subarachnoid space into multiple chambers. The bulbar segment has the maximum diameter and has a distinct anatomy compared to the rest of the optic nerve sheath. This part of optic nerve sheath plays a major role in the CSF flow dynamics between the optic nerve sheath and the subarachnoid space.

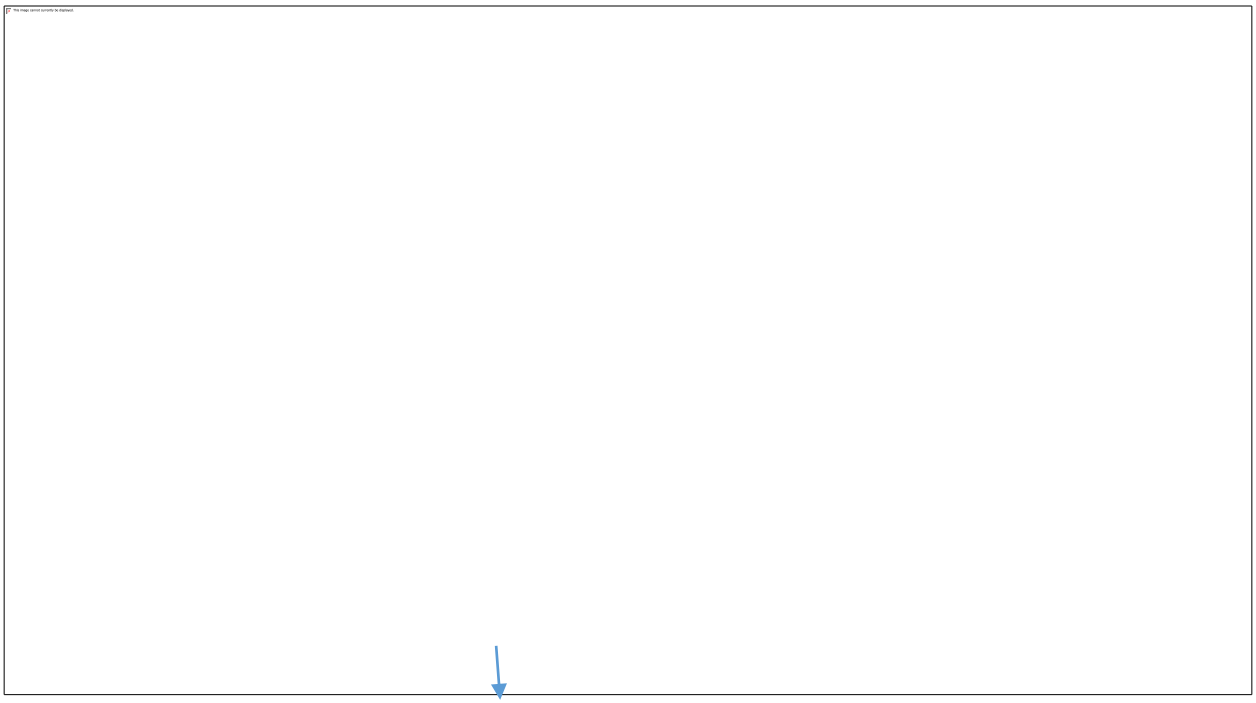


Figure 3 Optic nerve sheath microscopic anatomy showing trabecular pattern in the bulbar portion of the optic nerve sheath

It is proven by studies that cerebrospinal fluid (CSF) changes its direction of flow in the bulbar portion of the optic nerve sheath to return back to the site of absorption. Therefore this part of optic nerve sheath can be considered a blind sac where any change in the subarachnoid pressure inside the brain can cause direct changes thickness of the optic nerve sheath. In a cadaver study done by Liu and Kahn(5) it was found that the trabeculation rich bulbar segment of the optic nerve was the main part of optic nerve sheath which bulges and has the maximum diameter when they artificially created raised intracranial pressure. The increase in intracranial pressure causes distention of the optic nerve sheath in the bulbar segment due to

hydrostatic transmission of intracranial CSF pressure to the CSF in the subarachnoid space surrounding the optic nerve. This process happens in the optic nerve sheath long before the development of papilledema. (4). This increased CSF pressure in the subarachnoid space around the optic nerve causes increase in the diameter of the optic nerve sheath. Normally the volume of CSF in the optic nerve sheath is 0.1-0.2 ml. In one study it was found that when gelatin was injected into the optic nerve sheath in cadavers the bulbar part of the nerve which was 3 mm behind the globe had maximum distension. (6)

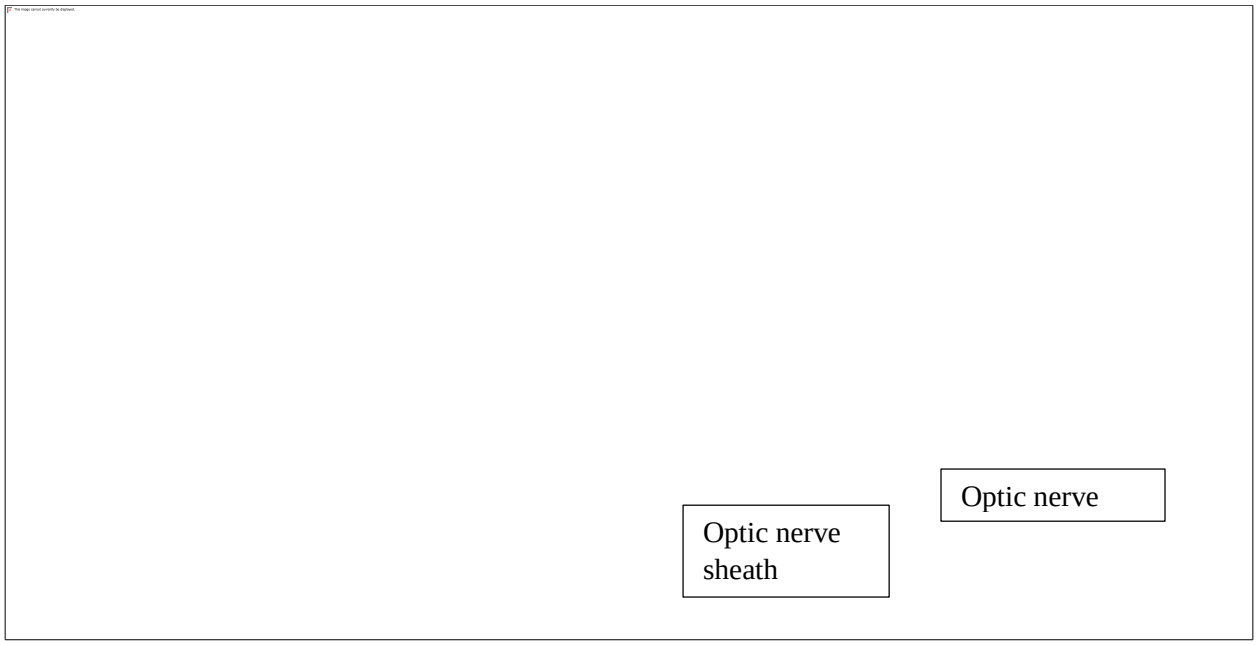


Figure 4 shows the part of the optic nerve sheath 3 mm behind the globe which has maximum diameter

In the above study it was also observed that, after injection of gelatin into the subarachnoid space the mean diameter of the optic nerve sheath increased by 60% at 3 mm behind the globe, but at 10 mm distance from the globe, the mean diameter only increased by 35%. There is another theory that CSF flow towards the ocular globe changes in direction due to the compression of the bulbar part of the optic nerve sheath due to eye movements. (5) In the bulbar part of the nerve sheath in patients with papilledema, reduced turnover of CSF was found, as well as a change in chemical composition of the CSF compared to the CSF in subarachnoid space in the brain. (1)

Measurement of optic nerve sheath diameter

Ultrasonographic visualization of the optic nerve has been well documented for the past three decades. As already mentioned above there are many studies which show a direct connection between optic nerve sheath subarachnoid space and intracranial pressure changes. (7)Since CSF can traverse in and out from the chiasmal cistern through the ONS, its diameter (ONSD) may be altered by changes in the pressure within the subarachnoid space. Thus measurement of ONSD by ultrasound may provide a clue to real-time changes in ICP. Papilledema is also a reliable indicator of raised intracranial pressure but it can take a few days to develop (8). Several methods may be used to measure ICP. Invasive intracranial pressure monitoring with an intraventricular catheter or pressure transducer is the most reliable way of measuring intracranial pressure but it has the disadvantage of being an invasive procedure which requires twist drill craniotomy or burr hole and may develop the complications of surgery like hemorrhage and infections. These invasive procedures also cannot be carried out in a patient having deranged bleeding parameters like thrombocytopenia, prolonged bleeding time or clotting time.

Optic nerve sheath diameter (ONSD) can be measured with help of magnetic resonance imaging (MRI) and in raised ICP, the ONSD has been found to be increased. In a retrospective study done by Geeraerts et al (9) in 38 patients it was observed that there was a significant positive correlation between the ONSD measurement by MRI and ICP measurement by invasive methods. They also found that the cut off value of 5.82 mm for ONSD has a sensitivity of 90% and specificity of 92% for detecting raised intracranial pressure above 20 cm of water. In a cadaveric study done by Steinborn at all (10) the optic nerve sheath

diameter was measured with help of high resolution ultrasound and MRI . Analysis at end of study showed that there was good correlation between the values measured by ultrasound and MRI.

In a retrospective study done by Hossein Kalantari (11) in 100 patients where ONSD was measured by computed tomography(CT) and MRI, it was observed that there was a good agreement between two values.. All the subjects had normal ONSD and the difference in the measurement of ONSD by CT and MRI was less than 0.2 mm. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) can be used to measure the optic nerve sheath diameter, but it has a disadvantage that patient should be shifted to respective centers or rooms for this procedure and it is also time-consuming. . A larger ONSD on MRI has been correlated with real time raised ICP measurement in patients with brain injury, but this may not be feasible at all times, particularly as a screening tool in a critically ill patient(9). Another disadvantage of use in MRI in measuring ONSD is that, it will not provide a real-time indication of ICP, as this is a dynamic variable.. Multiple studies showed that optic nerve diameter changes accordingly with raised intracranial pressure as proven by CT scans. (12)Ultrasonographic visualization of the optic nerve has been well documented for the past three decades. As already mentioned above there are many studies which show a direct connection between optic nerve sheath subarachnoid space and intracranial pressure changes. (7) Since CSF can move in and out from the chiasmal cistern through the ONS, its diameter (ONSD) may be altered by changes in the pressure within the subarachnoid space. Thus measurement of ONSD by ultrasound may provide a clue to real-time changes in ICP. Papilledema is also a reliable indicator of raised intracranial pressure but it can take a few days to develop (8). Several methods may be used to measure ICP. Invasive intracranial pressure monitoring with an intraventricular catheter or pressure transducer is the most reliable way of measuring intracranial pressure but it has the disadvantage of being an invasive procedure which requires twist drill craniotomy or burr hole, and is associated with the usual complications of surgery like hemorrhage and infections. Another disadvantage is that these invasive

procedures cannot be carried out in a patient with deranged bleeding parameters like thrombocytopenia, prolonged bleeding time or clotting time.

Ultrasonographic measurement of ONSD has the advantage of providing real-time assessment of ICP and it can be done at the bedside, even in a critically ill patient who may not be hemodynamically stable. Bedside ultrasonographic measurement of ONSD has been shown to be a non-invasive and reliable means to detect raised ICP in critically ill patients in several studies. (13) However, it allows only sequential measurement of ICP and does not reflect the continuous variations of the same. (13). A study done by Tayal VS et al (12) showed that the sensitivity of ultrasound in measuring raised intracranial pressure was 100% and the specificity was 63%. At the same time, the sensitivity of CT scan in detecting raised intracranial pressure was 84% and the specificity was 73%. (12) Another advantage of ultrasound in measuring optic nerve sheath diameter is that the learning curve of this method is very fast. There is one study which showed that an experienced radiographer will need only 10 measurements to get a good value and inexperienced operator only need 25 measurements to get a good result. (14)

The measurement of the ONSD has been standardized by several authors. A mode of ultrasound has been using since 1970 and B mode of ultrasound was introduced for the screening of intraocular pathologies since the 1980's. (13) Optic nerve sheath diameter is using a 7.5MHz linear transducer probe. The patient is placed supine and a thick layer of gel is applied above the upper eyelid and transducer is placed on the upper eye lid. The ONSD is measured 3 mm posterior to the globe. There are many studies which show that the part of the optic nerve 3 mm behind the globe has the maximum distension when the subarachnoid space was filled with gelatin. It was observed that optic nerve increased its diameter by 60% 3 mm behind the globe. There was only 35% increase in the diameter of the optic nerve 10 mm behind the globe (6).

In the ultrasonographic measurement of ONSD the ocular globe is seen as a prominent structure and is divided into two compartments by the lens. The lens appears as hypoechoic area in the ultrasound. The

optic nerve appears as a hypo-echoic structure surrounded by a hyper echoic layer of the thin piamater and the inner arachnoid layer. The CSF surrounding the nerve is hypo echoic and outer border of subarachnoid space and the optic nerve sheath appears as hyper echoic area. The hypo echoic subarachnoid space along with hyper echoic inner and outer nerve sheaths have to be clearly seen in the image for measuring the ONSD. The ONSD measurement is done by placing the markers on the border between the hypo echoic subarachnoid space and hyper echoic duramater. (10)

In a study done by Shah in 20 healthy volunteers, right eye ONSD was measured with 10-5 MHz ultrasound probe using the axial technique. The ONSD was repeated in the same eye using 10-5 MHz ultrasound probe by axial technique and intracavitary 8-5 MHz ultrasound probe using the coronal technique. Analysis at the end of the study concluded that inter-observer variability was very less in intracavitary method (13,15).

Relation between optic nerve sheath diameter and intracranial pressure

The optic nerve sheath diameter (ONSD) was found to be a sensitive indicator of increased intracranial pressure. In one study where the optic nerve sheath diameter measured by T2weighted MR images was compared with intracranial pressure which was measured using intra-parenchymal probes, it was found that diameter of the nerve less than 5.3 mm was unlikely to be associated with increased intracranial pressure and diameter of the sheath above 5.82 mm was associated with 90% probability of having increased intracranial pressure.(9) In a study done by Geerats et al(14) where ultrasound was used to measure optic nerve sheath diameter and this value was compared with intra-parenchymal pressure measured using a pressure transducer inserted by the neurosurgeon into the frontal lobe during surgery, it was found that the optic nerve sheath diameter cut-off value was 5.8 mm and the ONSD had a good correlation with raised intracranial pressure. The negative predictive value of test was 0.06 indicating that

there is very low chance of having raised intracranial pressure if one has an optic nerve sheath diameter less than 5.8 mm.

Watanabe A et al (16)in his study found that there was a good correlation between the optic nerve sheath diameter and the pressure of the subdural hygroma fluid. At the end of the study it was concluded that the optic nerve sheath diameter can be used as an indicator to differentiate between the raised intracranial pressure due to subdural hygroma causing mass effect on the underlying brain when compared to the subdural hygroma which develops due to cortical atrophy.

Dubos et al (17) in a study found that there was an increase in optic nerve sheath diameter measurement in patients with intracranial hypotension after they underwent epidural blood patch at the site of CSF leak. This was based on the theory that post lumbar puncture headache develops due to intracranial hypotension. In ten patients who developed post lumbar puncture headache, ONSD measurement was done by ultrasonography at a specific time prior to epidural blood patch and post procedure. Nine out of ten patient had significant improvement in a headache after the procedure and it was found that there was a significant improvement in ONSD after the procedure thus proving again that ONSD measurement is a surrogate marker of intracranial pressure.

In another study done by Dubos et al (18) where he compared the ONSD values of preeclamptic patients with healthy pregnant ladies, it was found that ONSD values were higher in preeclamptic patients. This study was based on the hypothesis thatpreeclamptic patients have higher intracranial pressure than healthy pregnant women and the main aim of the study was to find the incidence of raised intracranial pressure in preeclamptic patients. Twenty-six patients were included in the preeclamptic group and ONSD was measured with help of ultrasound in these patients. Twenty-five healthy pregnant women were taken as the control group and ONSD was done using ultrasonography. At the end of the analysis, it was found that 5 patients out of 26 patients with preeclampsia had ONSD values more than 5.8 mm and none of the

healthy pregnant women had an ONSD value of 5.8 mm or more. It was also found that on the third day after delivery those patients who had preeclampsia, had a significant decrease in the ONSD values when compared to the pre-delivery values thus again showing the correlation of ONSD with raised intracranial pressure.

Studies show that ONSD done by single investigator has high specificity and sensitivity thus indicating that ONSD can be used a good monitoring device in areas where no other methods of intracranial pressure monitoring are available.

In a study done by Frumin et al(19) where ONSD was done by a skilled operator on 27 trauma patients and those values were compared with values of intracranial pressure measured by an invasive intracranial pressure monitor, it found that ONSD ≥5.2 mm was a good predictor of elevated intracranial pressure (>20 mmHg) with a sensitivity of 83.3% (95% CI=35.9% to 99.6%) and specificity of 100% (95% CI=84.6% to 100%) and Spearman rank correlation coefficient of ONSD and ICP was 0.408 (p=0.03), demonstrating a moderate positive correlation.

In a prospective study done by Afshin Amini et al (20) ONSD measurement using ultrasound was done in 50 patients who were candidates for lumbar puncture for other diagnostic purpose. The ONSD measurements were done before and after the lumbar puncture. The ONSD in each eye was compared with the intracranial pressure obtained during the lumbar puncture. At the end of study it was observed that mean ONSD for the patients with raised intracranial pressure and normal individuals were 6.66 ± 0.58 and 4.60 ± 0.41 mm. Analysis at end showed that the mean ONSD above 5.5 mm can predict a raised intracranial pressure more than 20 mm of water with a sensitivity and specificity of 100%

In an another study conducted by Bauer J and Nedelmann M(21), they correlated the optic nerve sheath diameter(ONSD) measurements with raised intracranial pressure in patients with idiopathic intracranial hypertension(IIH) and response of the ONSD after lumbar puncture. Ten patients with idiopathic intracranial hypertension were selected for the study and twenty-five patients with other neurological disorders were selected as the control group. On analysis, they found that patients with IIH had increased ONSD in both eyes when compared to the control subjects (6.4 ± 0.6 mm vs. 5.4 ± 0.5 mm in controls; $p < 0.001$). They also found that the cut-off value of ONSD in detecting raised intracranial pressure was 5.8 mm. This value showed a sensitivity of 90% and specificity of 84% in detecting raised intracranial pressure. In all patients with IIH they did a lumbar puncture and found that there was a significant reduction in the ONSD after the procedure. Thus this study proved that ONSD can be used as a good method for monitoring treatment effects.

Experimental studies in ex vivo preparation of human optic nerves have shown that the ONSD measurements increase as the sheath is distended with fluid, akin to the condition when ICP is raised. It has been shown that ONSD returns to baseline within a few minutes, when the ICP returns to normal, provided the pressure is not increased beyond 45 to 55mmHg(4).

In a study conducted by Moretti and Pizzi(13), children below 4 years and adults were studied separately and they found that children more than 4 years of age and adults have ONSD up to 5mm while it is less than 4mm in children less than 4years of age.

Geerearts et al(14) demonstrated that an ONSD measurement of <5.7mm had a sensitivity and negative predictive value for high ICP of 100%. In a blinded study wherein ONSD measurements were performed in patients with suspected raised ICP, there was a good correlation between an elevated ONSD and findings of increased ICP on CT with a sensitivity of 93% and specificity of 100%.

In another similar study done on 26 patients by Major R , Girling S and Boyle A(22), it was found that ONSD measurement of>5mm in adult patients had a sensitivity of 95% and specificity of 100% when correlated with CT scan findings of raised ICP in a cohort of patients presenting to the emergency department with suspected intracranial pathology.

In a review of literature that included studies that correlated ONSD measurements with direct as well as estimated ICP measurements, the pooled sensitivity of ONSD was found to be 86.7% and the pooled specificity was 79.7%.(13).

However, in a cohort of children with craniosynostosis, ONSD measurements were shown to have a sensitivity of only 11% with a specificity of 97% when compared with presence/absence of papilloedema (23).

In another cohort of patients with hydrocephalus, children with symptoms of shunt malfunction requiring shunt revision had a significant rise in ONSD measurement from their own baseline measurement as compared to asymptomatic children with functioning shunts, even if the ventricular dilatation did not show significant change on imaging (24). A significant reduction in the ONSD measurement on MRI, although it did not return to baseline, was observed in children (who had no clinical signs of raised ICP) treated with endoscopic third ventriculostomy or tumor removal for hydrocephalus. The average value of preoperative ONSD was 6.21 versus 5.71 mm postoperatively (25).

ONSD measurements have been correlated with estimated ICP using middle cerebral artery blood flow velocity. In a study conducted by Soldatos et al (26) seventy six patients in ICU were studied. 50 patients with head injury were taken as study sample and 26 patients having no intracranial pathology were taken as control subjects. The patients were divided into two groups

based on Glasgow Coma Scale and semi quantitative neuroimaging Marshall scale. The patients having Marshall Scale I and Glasgow Coma Scale >8 were included in the moderate brain injury group and patients having Marshall Scale II to VI and Glasgow Coma Scale < or =8 were included in severe brain injury group. All these patients underwent intracranial pressure measurement by transcranial Doppler and ONSD measurements by optic nerve ultrasonography. Finally all patients underwent invasive intra-parenchymal intracranial pressure monitoring. Analysis of results showed that ONSD and intracranial pressure measured by transcranial Doppler were increased in patients with severe brain injury when compared to the patients with moderate brain injury and control subjects. They also found that ONSD has a very strong co-relation with estimated intracranial pressure found by transcranial Doppler (r 0.80 and $p< 0.0001$). In this study ONSD also showed good correlation to neuroimaging Marshall Scale (r 0.82 and $p< 0.001$). Final analysis showed that there was good correlation between the ONSD values and intra-parenchymal intracranial pressure monitoring values r 0.68 and $p= 0.002$ (26).

Ultrasonographic ONSD measurements have been reliably correlated with measurement of the diameter on CT. In a study done on complex or syndromic craniosynostosis where ONSD measurements done by ultrasound was correlated with ONSD measured on CT images, it was found that there was good correlation between the CT measurements and the ultrasound measurements of ONSD with r 0.41 and $p<0.001$. (23)

All these studies have showed that ONSD is a very good indicator or real-time changes in intracranial pressure. But there are also few limitations for ONSD. It has also been documented that optic nerve trauma and focal masses directly compressing the optic nerve could lead to false positive high ONSD measurements and ONSD is an unreliable predictor of raised ICP in such settings. Conditions like glaucoma, sarcoidosis, Graves' disease and tumors of the orbit may not

give a correct measurement of the optic nerve sheath. In such conditions the ONSD will not be a good method of assessing raised intracranial pressure.

Complications and limitations of ultrasound in measurement of optic nerve sheath diameter

There are no proven complications of ultrasound studies of the orbit. One theoretical complication is heating caused by the probe. There are no reported cases till now which had a major issue with this complication, and this can be avoided by keeping the ultrasound output power as low as possible.

Another drawback of ultrasound is that it cannot be used to measure ONSD in intraorbital pathologies like neoplasms, inflammatory diseases affecting the orbit, pseudo tumorcerebri and any extrinsic compression on the optic nerve caused by tumors.

A major technical problem with ultrasound is the formation of shadowing artifact. This is mainly due to the artifact arising from the lens and the optic disc, which projects as a hypo echoic band. An inexperienced observer may mistake this as the optic nerve sheath and will end up in the wrong measurement. One way of avoiding this artifact is the usage of curvilinear intracavitary probes and to do ultrasound screening in a coronal plane view. But as mentioned above the learning curve for doing this technique is rapid an observer with minimum experience will be able to avoid all these complications.

Raised intracranial pressure and decompressive craniectomy

Persistent elevation of intracranial pressure which is unresponsive to medical management is the most common cause of morbidity and mortality in patients with severe traumatic brain injury. It is proven by studies that an intracranial pressure more than 20 mm Hg that is not responding to medical measures resulted in a mortality of 100%(27). In patients with unilateral hemispheric or global brain swelling after traumatic brain injury, persistent intracranial hypertension is a bad sign for the patient. In spite of medical measures like anti edema drugs and other methods like pentobarbital coma, hyperventilation, these patients have a high mortality rate. In this type of patients, decompressive craniectomy becomes the only way to save life and reduce the raised intracranial pressure.

Various studies like the European Stroke Trial have shown that decompressive craniectomy can reduce mortality compared to the medical management in a patient who has brain edema secondary to ischemic stroke. There is however no conclusive proof that decompressive craniectomy benefits the patient. In DECRA, a major randomized controlled trial of decompressive craniectomy (decompressive craniectomy in patients with severe traumatic brain injury) it was found that patients who underwent decompressive craniectomy for diffuse traumatic brain injury have worse outcomes than the patients who was medically treated.

The main pathophysiology of the raised intracranial pressure is the increase in the total brain water content. There are many factors causing this cytotoxic edema like ischemia and low energy production at the mitochondrial level. When medical methods fail to control this process of edema the intracranial pressure rises. The main advantage of decompressive craniectomy at this stage is that it reduces the intracranial pressure independent of the biochemical changes. There are studies which show that decompressive craniectomy patients have improved compliance against intracranial volume challenges when compared

with patients with an intact skull. It is also proven that decompressive craniectomy improves the cerebral blood flow and reduces the amplitude of the intracranial pressure waves. Hence the overall outcome after decompressive hemicraniectomy is good in those patients whose intracranial pressure was uncontrolled with medications.

Effect of Trendelenburg and reverse Trendelenburg position on intracranial pressure

There are various studies showing that Trendelenburg (head end 30 degrees down) and reverse Trendelenburg (head end 30-degree elevation) has significant effects on the intracranial pressure. In a study done by Mavrocordatos et al (28) in 15 patients posted for elective intracranial surgery, the intracranial pressure was monitored with help of lumbar puncture needles inserted into spinal thecal sac at L3-4 vertebral level after confirming free CSF circulation between the intracranial compartment and the spinal subarachnoid space. The lumbar puncture needles were connected to the pressure transducer and continuous intracranial pressure was recorded. Each patient was positioned in operating table in three different positions, horizontal (0-degree head end elevation), Trendelenburg and reverse Trendelenburg position and intracranial pressure was measured. A central venous catheter was also inserted into the right jugular vein for continuous measurement of central venous pressure. On analyzing the data it was observed that there was a significant increase in the intracranial pressure and central venous pressure in Trendelenburg position. This can be explained by theorizing that Trendelenburg position reduces cerebral venous drainage, resulting in an increase in cerebral venous blood volume and increase in ICP(28).The reverse Trendelenburg position has been used in critical care and neuroanesthesia to reduce intracranial pressure. The main advantage of this position is that the intracranial pressure is reduced without any effect on the cerebral perfusion pressure. (29,30)

Complications following decompressive craniectomy

There are many complications following decompressive craniectomy. In a retrospective study done in 41 patients the main complications were as follows: 51% of the patients developed herniation of the cerebral cortex through the craniectomy defect, 62% developed subdural effusions, 14% of patients developed seizures and 11% developed hydrocephalus (31). Other rarer complications following this procedure were worsening of hemorrhagic contusions(32), development of contralateral subdural hematomas(33) and CSF circulation derangements. In a retrospective study done by byHoneybull et al(31) in 164 patients who had a decompressive craniectomy for severe head injury from 2004 to 2009 eighty-six patients had a bifrontal decompression and seventy-eight had a unilateral surgery. Complications due to the decompressive surgery were, herniation of the cerebral cortex through the bone defect (42 patients, 25.6%), subdural collection of blood or CSF (81 patients, 49.4%), seizures (36 patients, 22%), hydrocephalus (23 patients, 14%), and syndrome of the trephined (2 patients, 1.2%)

Herniation of the cerebral cortex commonly occurs after the surgery as can be considered as a natural phenomenon after the procedure. This herniation of can cause contusions in the brain at the edge of craniectomy defect which is difficult to differentiate from old contusions that are undergoing maturation. Performing an adequate and extensive craniectomy flap is the only way to reduce this complication.

Post-decompressive craniectomy subdural collection or effusion is the next major complication after this procedure and is mainly due to rupture of the veins between the duramater and the arachnoid interface and trabeculae and the transient dynamic changes seen in CSF circulation. It occurs mainly after severe head injury and there are studies which showed a correlation of development of subdural collection and severity of head injury(31). The subdural collection is self-limiting and resolves completely after replacement of the bone flap.

Post-traumatic hydrocephalus develops in 0.7 to 29% of patients with head injury. The formation of subdural and subglacial effusions develops due to disturbances in CSF flow after severe head injury. In addition to the post traumatic CSF flow disturbances decompressive craniectomy also alters the CSF flow along with subarachnoid scarring which contributes to the development of hydrocephalus.

In patients with severe head injury who undergo decompressive craniectomy the incidence of seizures was found to be 22%. (31, 34) The impact of head injury and the cerebral manipulation during decompressive craniectomy may be the reason for these seizure episodes. In an, another study done by Annegers et al (35) in patients with severe head injury the incidence of seizures was found to be 10-15 % for adult patients and 30-35 % for children. It was also observed that the relative risk of seizures was 1.5 in mild injuries 2.9 after moderate injuries and 17.2after severe injuries.

Another major complication which occurs late after this procedure and is of interest in our study is the Syndrome of the Trephined.

Syndrome of the trephined

The term “syndrome of the trephined” was coined by Grant et al in 1939. This syndrome consists of reversible neurological and behavioral disturbances which develop after craniectomy. This syndrome described by Grant et al was attributed to the “sense of vulnerability” due to lack of cranial vault resulting in psychiatric symptoms. (34)

This syndrome has a close association with another entity called the syndrome of the sinking skin flap which was described by Yamaura et al.(36) This syndrome has many clinical

manifestations like seizures, psychiatric disturbances, focal motor deficits, headache and a feeling of uneasiness at operated site.

Rare manifestations of this syndrome include midbrain dysfunction and clinical symptoms of Parkinsonism. There is a case report of a patient who underwent decompressive craniectomy, who later developed midbrain dysfunction in the form of extra ocular movement disturbances along with neuropsychiatric deficits, fatigue and headache. This patient underwent cranioplasty after which he had significant improvement in these symptoms. (37) Another patient who developed bradykinesia, dysarthria, and levodopa-resistant Parkinsonian tremors 4 weeks after decompressive craniectomy. These symptoms worsened when the patient was made to sit upright. This patient also underwent cranioplasty after which he had significant improvement in these symptoms(38).

Sydney did a retrospective study in 29 patients who underwent decompressive craniectomy. The main aim of the study was to find the prevalence of syndrome of the trephined and its association with demographic information, clinical symptom patterns and radiological signs. Analysis of data at end of study showed that 24% of patients developed the syndrome of the trephined. This was against an incidence rate of 1.2% which was reported in a retrospective study done by Honeybul et al.(34) In terms of clinical symptoms in the syndrome of the trephined, it was found that chronic rehabilitation arrest was the most common symptom rather than acute neurological decline. In the same study, they found out that craniectomy size and the age of the patient did not have any statically significance in the development of symptoms. In terms of radiological features, they found that sunken skin flap contour was the most sensitive sign for the development of this syndrome.

The syndrome of the sinking skin flap was described as the objective neurological abnormalities which can be explained only due to the concavity of the skin flap and the atmospheric pressure acting on the underlying cerebral cortex. His study also confirmed the theory put forward by Fodstud et al which concluded that only symptoms which reduce or are relieved by cranioplasty should be included in the syndrome of the trephined. Thus the post traumatic syndrome which was associated with subjective symptoms not the neurological deficits of the patients became a separate entity from the syndrome of the trephined.

There is also an entity called motor trephined syndrome which consists of only motor deficits which develop late after decompressive craniectomy and are relieved after cranioplasty surgery. The motor trephine syndrome was studied by Silvers et all in which 20% of his patients who underwent decompressive craniectomy developed contralateral upper extremity weakness 5 months after the surgery. These patients underwent cranioplasty and 72 hours after the surgery these patients had significant improvement in the motor weakness. CT perfusion scan done in these patients showed significant improvement in the cerebral blood flow along with normalization of the cerebrospinal fluid flow disturbances.

There are many studies which support the fact that syndrome of the trephined has a very close association with head posture of the patient and cranioplasty surgery(38). Many patients with this syndrome showed significant improvement in speech and hemiparesis after placing the patient in horizontal or Trendelenburg position. In a case report, one patient who underwent decompressive craniectomy had significant improvement in the Parkinsonian tremor when he was made to lie down.

Physiological changes in patients with large cranial defects

In patients with large cranial defects following decompressive craniectomy, as for trauma or malignant cerebral swelling, the atmospheric pressure directly affects ICP. This results in "syndrome of the trephined" or the "syndrome of the sinking flap", wherein ICP is raised as the head end is elevated and it falls as the head end is lowered. (16)This occurs usually about 4 to 5 months following removal of the bone flap. (39)Patients with this syndrome manifest with fall in GCS score/development of focal neurological deficits in the upright position that is relieved on lowering the head end(39,40). These manifestations have been attributed to direct compression of the cerebral cortex by the in folding scalp flap(41), changes in cerebral blood flow in relation to posture and influence of atmospheric pressure on the cranial defect, or changes in CSF hydrodynamics due to the atmospheric pressure directly acting on the cerebral cortex. (40,42) The various theories are explained in detail below.

Effect of atmospheric pressure on the cerebral cortex

After the decompressive craniectomy, the "closed box "concept of the skull is no longer valid and the principles of Monroe-Kellie become invalid. The atmospheric pressure acts on the cerebral cortex in the open box causing multiple deficits which are seen in the syndrome of the trephined. This atmospheric pressure also acts on deep structures in the brain like basal ganglia, brain stem causing symptoms like headache, Parkinsonian tremor and multiple cranial nerve palsies(38).

Disturbances in CSF low dynamics after decompressive craniectomy

In an open cranial cavity, the intracranial pressure tends to equalize with the atmospheric pressure, resulting in high intracranial pressure than normal. This change in intracranial pressure has been demonstrated in a study done by Fodstad et al (42) in which CSF hydrodynamics was studied with help of CSF infusion tests. In that study author compared the CSF hydrodynamic variables with clinical signs of the patient and found that patients who had clinical improvement in the syndrome of trephine after cranioplasty also had improvement in CSF hydrodynamic variables like resting pressure, sagittal sinus pressure, buffer volume, and pulse variations at resting pressure. The development of subdural hygromas after a head injury can also be explained by the same mechanism of altered CSF flow dynamics after the injury in which abnormal collection occurs in the space between the duramater and the underlying arachnoid. The alteration in CSF flow along with increased resistance to CSF out flow caused by mechanical or inflammatory blockage of subarachnoid spaces has been postulated as the possible mechanism of post-traumatic hydrocephalus(42).

Alteration of cerebral blood flow and metabolism

Various studies have shown that there are variations in the cerebral blood flow and metabolism after decompressive craniectomy. In a study done by Yoshida et al on seven patients who underwent decompressive craniectomy for raised intracranial pressure following subarachnoid hemorrhage, it was found that there is a significant improvement in the cerebral blood flow and metabolism after cranioplasty. The cerebral blood flow and metabolism were evaluated using 133 Xe-CT and 31P magnetic resonance spectroscopypre and post-cranioplasty. It was also found that after cranioplasty the cerebral blood flow to the deep structures like thalamus

normalized after the surgery. In the imaging done using magnetic resonance spectroscopy, it was found that phosphocreatine to organic phosphate ratio which is a sensitive indicator of cerebral energy metabolism improved after cranioplasty. (43) Transcranial Doppler which is useful in measuring cerebral blood flow also showed significant improvement in the blood flow in the cerebral cortex in patients after cranioplasty. (44) CT perfusion studies also showed that there is a significant improvement in the cerebral blood flow after the cranioplasty. These studies all confirm that in patients with the syndrome of the trephined there is a considerable decrease in the cerebral blood flow and metabolism. The exact mechanism for this reduced blood flow is not understood, but various theories state that compression of the unfolding flap on the underlying cerebral cortex reduces the vascular flow and reduces the venous return. The mechanism of improvement in the blood flow in the deep structures like thalamus can be explained by mechanisms like improvement in the auto regulatory function and reduction in the cerebrovascular resistance after cranioplasty.

It has been proven by 18-FDG PET-CT imaging studies that there is significant impairment in the cerebral metabolism in patients having hemicraniectomy defect and significant improvement in the cerebral metabolism after the cranioplasty surgery. (45)

Management of syndrome of the trephined

The management of this condition is by providing a covering of the defect in the vault (cranioplasty) so that the atmospheric pressure cannot influence the ICP(40,42,44). It has been demonstrated that cranioplasty can restore cerebral blood flow dynamics as well as normalize CSF pressure. (46)

It may be noted that not all patients with cranial defects manifest this syndrome. In one series, reversible monoparesis attributable to the syndrome of the trephined that was successfully treated with cranioplasty

was observed in 26% of 38 patients who were readmitted for cranioplasty following decompressive craniectomy for traumatic brain injury. (39) Apart from motor deficits which can be objectively assessed, several subjective symptoms such as giddiness, vague sensation over the craniectomy defect, headache have been recorded to have been reversed with cranioplasty in patients with decompressive craniectomy skull defects. (42) As several of these non-motor symptoms may be attributable to the subjective feelings following craniotomy, the exact incidence of the syndrome of trephined is difficult to estimate. In one series, the incidence of the syndrome of the trephined in patients following decompressive craniectomy was reported to be only 1.2%. (31,34)

A review of the literature suggests that a rise in ICP in relation to an upright posture can result in motor as well as non-motor symptoms in patients with large skull defects. While reversibility of a motor deficit with a change in posture may be easy to document preoperatively before cranioplasty, the role of cranioplasty in reversing non-motor symptoms cannot be easily predicted. It has been proven by studies that increase the intracranial pressure caused by the pressure of the unfolding skin flap is a major cause of neurological deficits in the syndrome of trephined and cranioplasty is the treatment of choice to relieve this pathology caused by atmospheric pressure effects. Measurement of ONSD as a surrogate marker of raised ICP could be useful in this subgroup of patients in counseling them regarding whether cranioplasty may benefit them or not. With this background, we aim to measure ONSD using orbital ultrasound in patients admitted for cranioplasty to cover large skull defects following decompressive craniectomy for traumatic brain injury and study if a variation in ONSD can be detected with changes in posture.

MATERIALS AND METHODS

This study was approved by institutional review board. This study is done in 2 groups. Normal healthy subjects working in the Department of Neurological Sciences in CMC Vellore and willing to volunteer for the study were included in the first study group. Patients who had undergone a decompressive craniectomy following traumatic brain injury are routinely screened in the Brain Injury Clinic and readmitted for cranioplasty. These patients were included as the 2nd study group. All the normal subjects and patients were included in the study after obtaining an informed consent.

Inclusion criteria

1. Normal subjects with no history of prior injury to the eye.
2. All patients undergoing cranioplasty for cranial defects following decompressive craniectomy for traumatic brain injury above the age of 18 years who are willing to participate in the study.

Exclusion criteria

1. Previous surgical procedures in the eye or CSF diversion procedures.
2. All patients less than 18 years of age.
3. Patients who have evidence of bilateral optic nerve dysfunction/injury.
4. Patients in whom ultrasonography could not be reliably performed due to excessive movement of the eyeball

Location of study

The study was conducted in Neuro high dependency area (NHDA) and Neuro trauma ward.

Ultrasound machine used for the study

Sonosite Fujifilm M turbo Model portable ultrasound machine was used for the study.

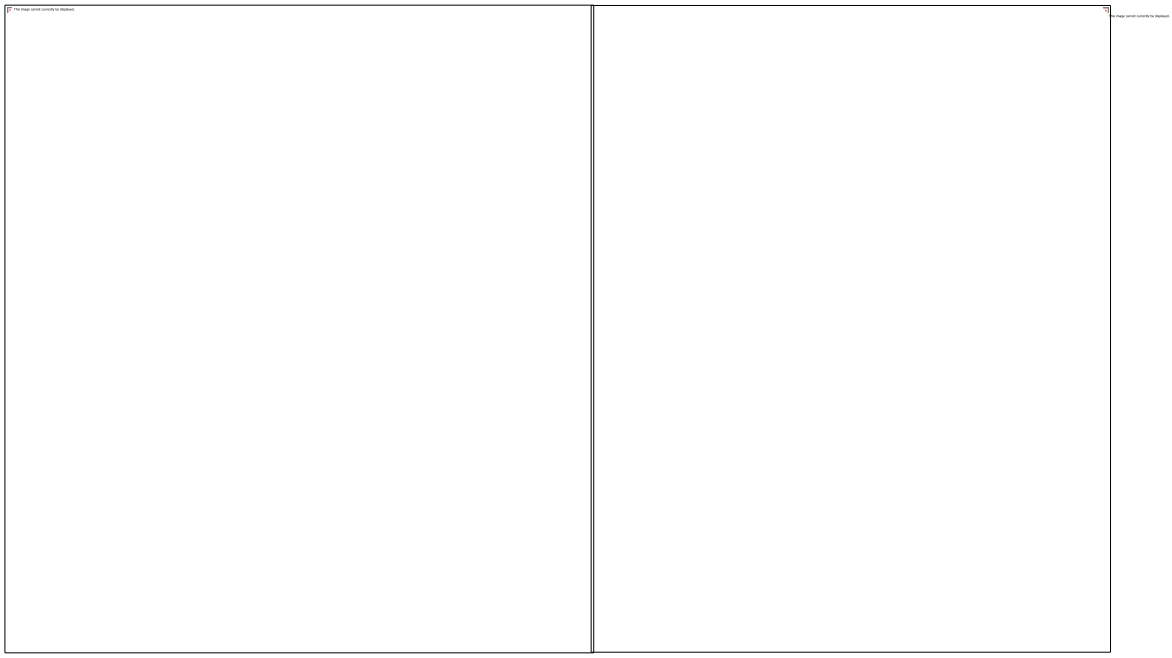


Figure 5 showing ultrasound machine(a) used in the study and the ultrasound probe(b)

Study Group 1

Ten normal subjects were included in the study. Each person was made to lie down on a bed. They were instructed to close their eyes and not to move the eye ball.

Initial ONSD reading was done by placing the subjects in supine position without any elevation of the head. The name and the hospital number were registered in the ultrasound machine before each study. The ultrasound probe is covered with gel and placed on the closed eyelid. The probe is adjusted to get a fairly clear image of the eye ball along with the optic nerve and optic nerve sheath. The optic nerve was visualized as a hypoechoic area surrounded by hyperechoic area and measurement of ONSD would be made 3mm posterior to the point in the axial plane at the globe where the optic nerve exits it. The measurements were repeated three times for each eye and the average of these six readings would be taken as the ONSD. The procedure was repeated after placing the subject in the reclining position with the head end elevated at 30 degrees for 30 minutes, and then after placing the patient for 30 minutes with the head end lowered to 30 degrees below the horizontal. The heart rate and the blood pressure were recorded during this procedure.

Measurement of ONSD in patients undergoing cranioplasty

The second study group consisted of patients admitted for cranioplasty. The patient was made to lie down supine for 20 minutes before starting the study. The patient would be instructed to not move the eyeball. The optic nerve sheath is visualized with ultrasound and diameter is measured 3mm posterior to the point in the axial plane at the globe where the optic nerve exits it. The measurements were repeated three times over each eye and the average of these six readings was

taken as the ONSD. The procedure was repeated after placing the patient in the reclining position with the head end elevated at 30 degrees for 30 minutes and placing the patient for 30 minutes with the head end lowered to 30 degrees below the horizontal. In patients who had concomitant unilateral traumatic optic neuropathy, the measurement would be performed only in the eye that has an intact optic nerve. In case there was extreme discomfort to the patient on lowering the head end to 30 degrees, measurement in this position was avoided and comparisons were performed on the measurements obtained in the other two positions alone (supine and head end elevation of 30 degrees).

The neurological status of the patient, non-motor symptoms such as vertigo or a headache related to posture, GCS score, and pulse rate were documented at the same time ONSD is determined. It was also noted if the flap was sunken or not.

For first 10 patients, the measurements were done by two observers, one set of readings by author and another set of readings by an experienced doctor who already had done a study on ONSD. The difference in measurements between these two observers was used to calculate the inter-observer variability.

Management

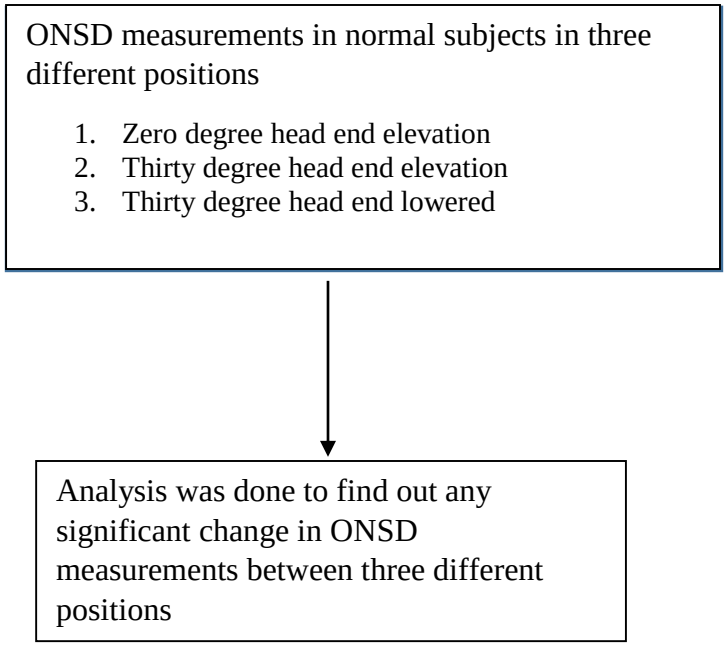
All patients recruited for the study were taken for cranioplasty under general anesthesia. Polymethyl methacrylate was used to make the bone flap in all the patients.

Post-operative measurement of ONSD in cranioplasty patients

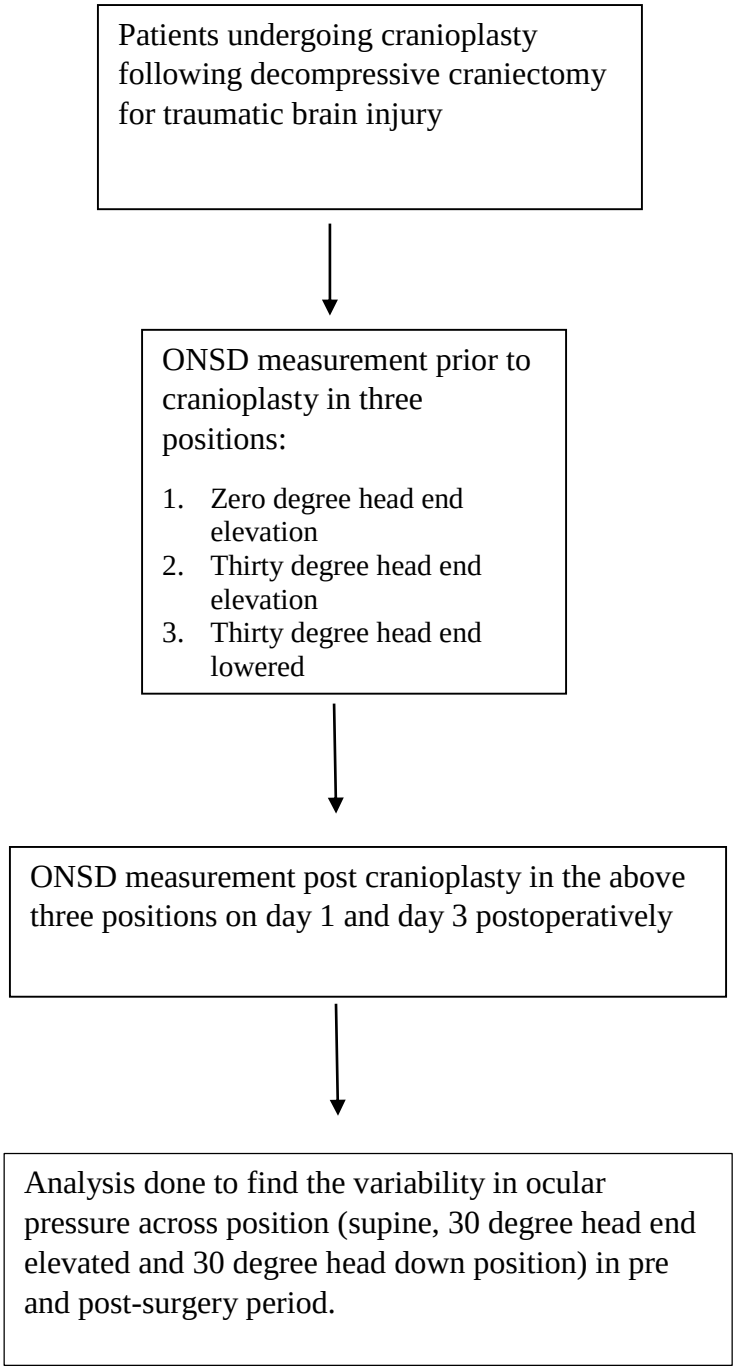
The ONSD measurement was done in the same way as described above in each patient on the first post-operative day and the third post-operative day. The patients were made to lie down in three positions, head end 0-degreeelevation, head end elevated 30 degrees above the horizontal level and head end lowered 30 degrees below the horizontal level. The measurements were taken after the patient had been in that position for 30 minutes, and repeated three times over each eye and the average of these six readings was taken as the ONSD.

Detailed diagrammatic Algorithm of the study

Study group 1



Study group 2



Data analysis

The analysis was done using STATA version 12 software. In the group 1 the mean ONSD in each position was calculated and comparison was made between values in each position using paired t-test. The mean ONSD value in the head end zero degree position was compared with the mean ONSD value in 30-degree head end elevation and 30-degree head down position. A p value of <0.05 was considered significant. The inter-observer variability was calculated for first 11 patient's data using Intraclass correlation coefficient (ICC) test.

In the second group we calculated the variability of ONSD values between pre-operative period and the third post-operative period. Variability in ocular pressure across position (elevated and down) in pre and post-surgery period were summarized using range (maximum minus minimum) as a summary statistic or measure.

RESULTS

Comparison of ONSD values in normal subjects in three positions (study group 1)

In the first study group all subjects were male and the mean age of the study group was 28 years. The mean ONSD value in 0 degree head end elevation was 5.02 ±0.15 and in 30-degree head end elevation and 30-degree head down position were 5.03±0.18 and 5.08±0.16 respectively. When the mean ONSD value in 0 degree head elevation was compared with that of 30 degrees head end elevation using paired t-test, the p-value was 0.6817 which indicates that the difference in the values was not significant. Similarly when we compared the ONSD in 0 degrees head position with 30 degree head down position the p-value was 0.060 again showing that the differences between values in these two positions are not significant. Overall analysis showed that there was no significant difference in the ONSD values in three different head end positions.

Table 1. ONSD measurements in normal subjects in the three different positions

ID	a	b	c	d	e	f
1	4.966667	5	4.933333	4.966667	5.033333	5.033333
2	5.233333	5.1	5.2	5.166667	5.333333	5.233333
3	5.233333	5.133333	5.2	5.2	5.133333	5.2
4	5.066667	5.033333	5.066667	5.1	5.133333	5.1
5	4.933333	5.033333	4.8	5.033333	4.9	5.033333
6	5.166667	5.2	5.333333	5.2	5.266667	5.166667
7	5.066667	5.166667	5.033333	5.066667	5.166667	5.066667
8	5.066667	5.033333	5.033333	5.1	5.166667	5.133333
9	4.866667	4.866667	5.033333	5.033333	5.233333	5.066667
10	4.7	4.666667	4.633333	4.6	4.533333	4.833333

a: 0 degree left eye, b: 0 degree right eye, c: 30 degree elevation left eye, d: 30 degree elevation right eye, e: 30 degree down left eye, f: 30 degree down right eye

Table 2 Comparison of mean ONSD value at 0 degree head elevation with 30 degree head end elevation and 30 degree head down position

0 degree, 5.02±0.15	30 degree up 5.03±0.18	P =0.6817
0 degree ,5.02±0.15	30 degree down 5.08±0.16	P = 0.060

Patient characteristics of study group 2

Out of the 29 patients recruited for the study 22 (75%) were males, with a median age of 28 years. Eighteen patients (62%) patients had left sided hemicraniectomy defects, 11 patients (38%) had right sided defects and 3 patients had bilateral frontotemporal craniectomy defects. Four patients (13%) had neurological deficits in the form of hemiparesis at admission, and none of the patients developed any new neurological deficits during the tests. Two patients had history suggestive of the syndrome of the trephined at the time of admission. 28 patients had a GCS score of 15/15 at the time of admission and one patient had GCS score of 13/15. The patient with GCS score of 13/15 improved to normal GCS after the surgery. Analysis showed that there was no significant change in the heart rate and blood pressure for all patients before and after the surgery.

Table 3 Baseline characteristics of patients in the study group 2

Variable	Proportion (%)
Age -Median (range)	28 years (19-55 years)
Sex - Male - Female	 22 (75.9%) 7 (24.1%)
Type of surgery - Frontotemporo-parietal - Bifrontal	 26 (89.7%) 3 (10.3%
Side of decompression - Right - Left	 8 of 26 (30.8%) 18 of 26 (69.2%)
GCS at admission - 15 - <15	 28 (96.5%) 1 (3.5%)
Pre-op motor deficits	4 (13.3%)
Syndrome of the trephined	2 (6.8%)

Flap positions in pre-operative patients and changes according to head position

For all patients in the preoperative period the craniectomy flap position was also noted in the three different head positions and recorded as either sunken or full. When the patients were made to lie supine with 0-degree head end elevation, we found that three patients (10.34%) patients had full flaps and in the rest of the patients (89.66%) the flaps were sunken.

Table 4 Flap positions in pre-operative patients

Flap	Number (%)
Full	3(10.34)
Sunken	26(89.66)

When these three patients were positioned with a 30degree head end elevation it was found that in two of them the craniectomy flap changed from the full position to sunken position.

Table 5 Comparison of 0 degree head elevation position 30-degree head end elevation position

Pre-op 0 degree Flap position	30 degree elevation		Total
	Full	Sunken	
Full	1	2	3
Sunken	0	26	26

When the 26 patients who had a sunken flap at 0degree head elevation position were made to lie down in a 30degree head down position, 24 (92.3%) patients' flaps changed from the sunken to full position.

Table 6 Comparison of flap position between 0 degree head elevation and 30 degree head down position

Pre-op 0 degree Flap position	30 degree down	30 degree down	Total
	Full	Sunken	
Full	3	0	3
Sunken	24	2	26

ONSD values in patients recruited for cranioplasty (study group 2)

Variability in ONSD measurement across positions (supine, elevated and down) in pre and post-surgery period were summarized using range (maximum minus minimum) as a summary statistic or measure. A patient with high variability in measurements across positions will have a higher range and likewise a patient with low variability will have a low range for pressure measured across three different positions. Theoretically, it was expected that the variability of the pressure measurement would decrease after the surgery when compared to measurements taken before the surgery.

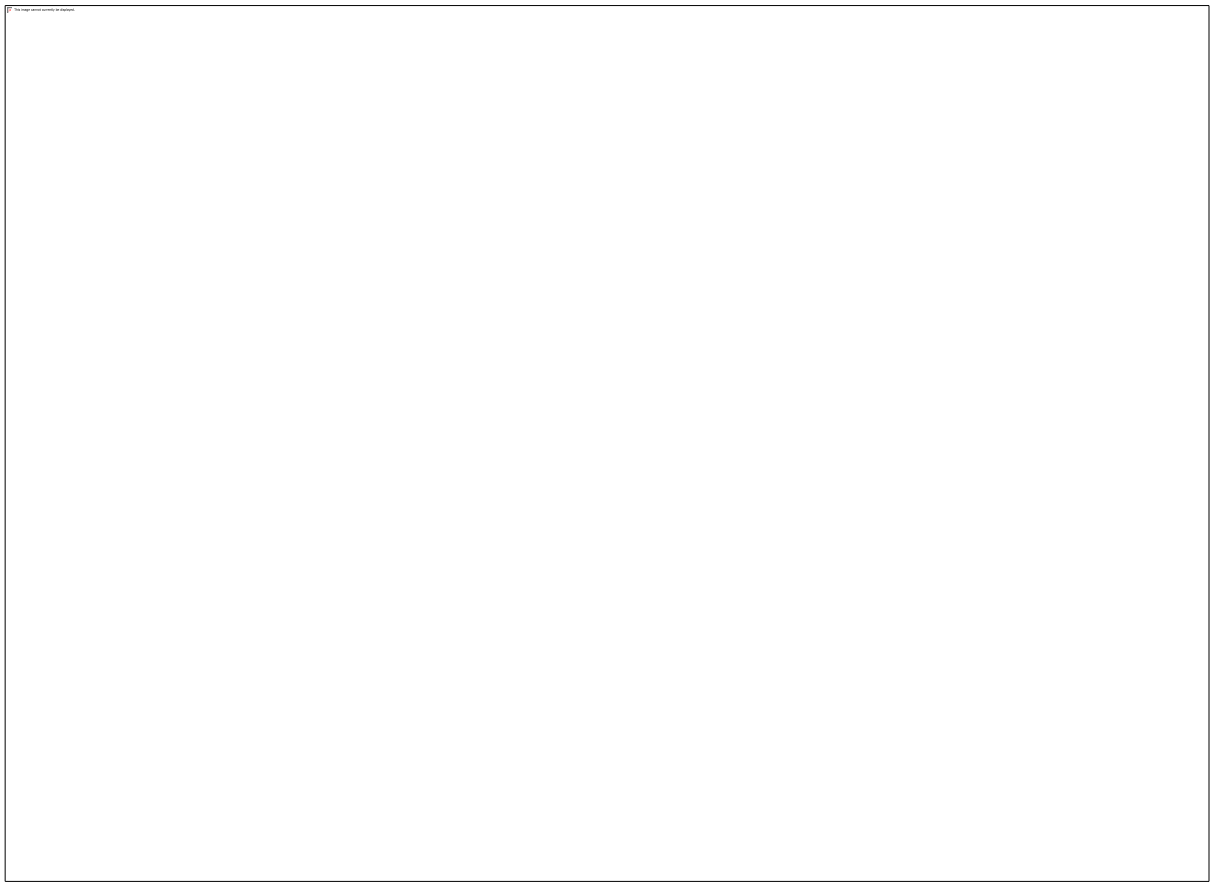
Table 7 Mean ONSD values of patients in pre-operative and post-operative period

Pre -operative patients (n=29)	Mean ONSD in mm
0 degree head end elevation	5.05
30 degree head end elevation	5
30 degree head end down	5.13
Post-operative patients (n=29)	
0 degree head end elevation	5.06
30 degree head end elevation	5.04
30 degree head end down	5.13

Table 8. Mean ONSD values categorized by positive or negative change in variability

Patients showing decrease in variability after surgery (n=17) Pre-operative	Mean ONSD in mm
0 degree head end elevation	5.1
30 degree head end elevation	5.09
30 degree head end down	5.23
Post -operative	
0 degree head end elevation	5.16
30 degree head end elevation	5.14
30 degree head end down	5.21
Patients showing increase in variability after surgery (n=12) Pre-operative	
0 degree head end elevation	4.97
30 degree head end elevation	4.88
30 degree head end down	4.99
Post -operative	
0 degree head end elevation	4.92
30 degree head end elevation	4.89
30 degree head end down	5.02

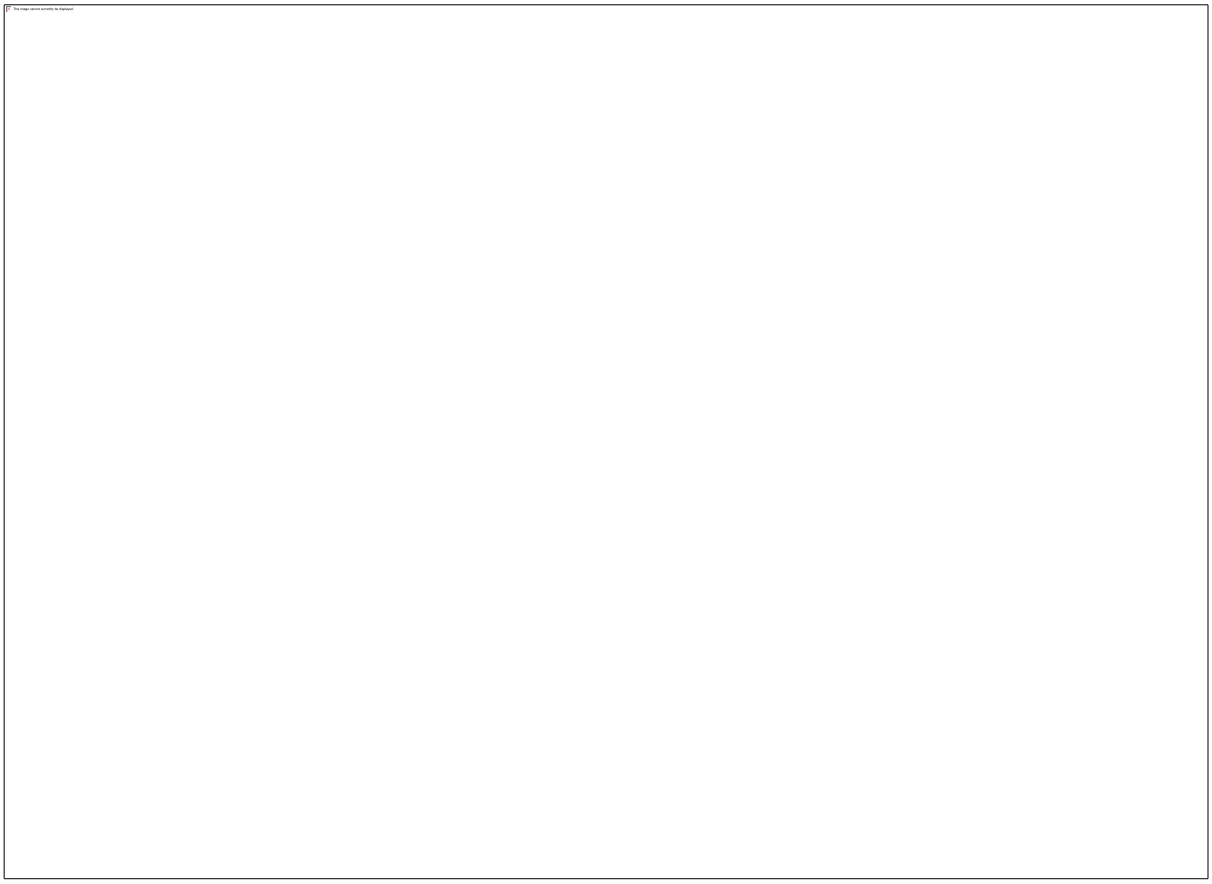
Fig 6. Comparison of range (as a measure of variability) of pressure measurements between pre-operative period and post-operative period (day 3)



The time period (pre – post) is represented in x-axis and the range (difference between the ONSD in head down and head up positions in millimeters) of measurements is shown in y-axis. The plot depicts the change in range of measurements for each of the study 2 sample subjects (n=29).

Based on the patterns observed in figure 5, the samples (n=29) were stratified into two groups: negative change (or samples which showed decrease in range after surgery, n=17) and positive change (or samples which showed increase in range after surgery, n=12). This plot shows the pattern of change in range of pressure measurements in each of the two sub-groups.

Figure 7: Comparison of range of pressure measurements in two sub-groups



Negative (n= 17)

Positive (n=12)

Total (N=29)

This analysis showed that 17 (58.6%) patients had decrease in the variability in the ONSD values after the surgery, of whom two patients had a marked decrease. The patient who showed maximum decrease was a 28 year old lady who underwent left fronto-temporo-parietal cranioplasty. Her pre-operative values in 30 degree head end elevation and 30 degree head down position was 4.1 mm and 4.75 mm respectively, a difference of 0.65 mm. ONSD measurement on the third post-operative day and found that her ONSD measurements in 30 degree head end elevation and 30 degree head down position were 4.45 mm and 4.65 mm respectively, a difference of only 0.2 mm.

Inter-observer reliability

Table 9 Inter-observer reliability.

	Obs1	Obs2	Diff(ds)	ICC
Pre 0 degree 30 degree elevation 30 degree down	 4.84 ± 0.27sd 4.73 ± 0.35sd 4.95 ± 0.27sd	 4.81 ± 0.32sd 4.76 ± 0.36sd 4.94 ± 0.278sd	 0.024 ± 0.095sd -0.022 ± 0.074sd 0.007 ± 0.050sd	 0.975 0.989 0.991
Post1 0 degree 30 degree elevation 30 degree down	 4.83 ± 0.25sd 4.80 ± 0.29sd 4.93 ± 0.32sd	 4.86 ± 0.23sd 4.81 ± 0.30sd 4.96 ± 0.31sd	 -0.024 ± 0.097sd -0.013 ± 0.062sd -0.031 ± 0.081sd	 0.960 0.989 0.982
Post 3 0 degree 30 degree elevation 30 degree down	 4.83 ± 0.27sd 4.80 ± 0.32sd 4.98 ± 0.30sd	 4.86 ± 0.25sd 4.83 ± 0.33sd 4.96 ±0.31sd	 -0.022 ± 0.092sd -0.036 ± 0.083sd 0.02 ± 0.071sd	 0.969 0.982 0.986

For 10 subjects the ONSD measurement was taken by 2 observers – the Principal Investigator and a senior faculty member of the Neuro ICU with several years of experience in the measurement. The interclass correlation coefficients (ICC) were calculated, with a higher ICC indicating higher agreement between the observers and a low ICC denoting no agreement between raters. The ICC values obtained were high, indicating good agreement between the two observers.

Illustrative case

Nineteen-year-old Mr X had sustained head injury following a road traffic accident on 15/12/2015. He had undergone left fronto-temporo-parietal decompressive craniectomy and left anterior temporal lobectomy on 16/12/2015 at CMC. His postoperative course was uneventful. There was no history of seizure or weakness in any of the limbs. He was currently admitted for cranioplasty. He did not have any known co-morbidities. His general examination and neurological examination was normal except he had mild upper motor neuron type facial paresis on the right side with pronator drift on the right side and rapid alternating movements were impaired in the right upper and lower limbs. The rest of the neurological examination was normal. The craniectomy flap was sunken. The wound had healed well. He underwent left fronto-temporoparietal cranioplasty on 11/01/2017. His postoperative course in the hospital was uneventful.

Pre-operative measurement of ONSD

Head end 0 degree elevation

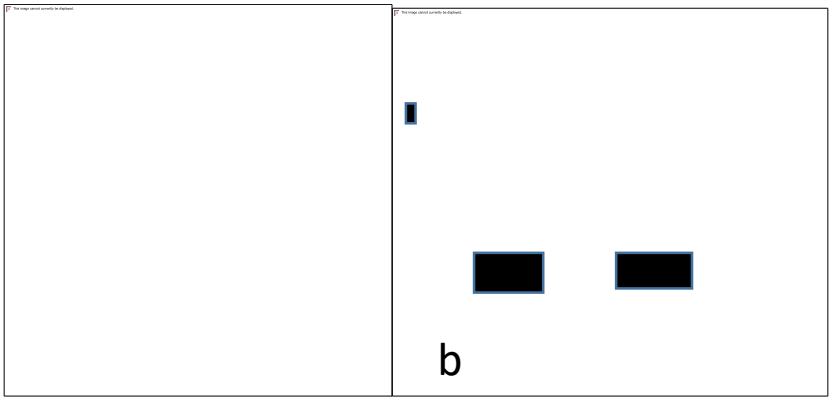


Fig 8 showing patient position in 0 degree head end elevation (a) and figure (b) showing a sunken flap

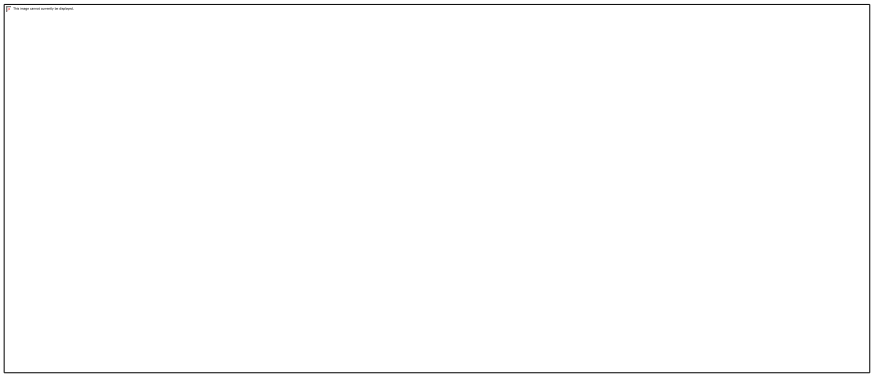


Fig 9 showing ONSD values in the left eye (a) and right eye (b) respectively

Head end 30 degrees elevated position

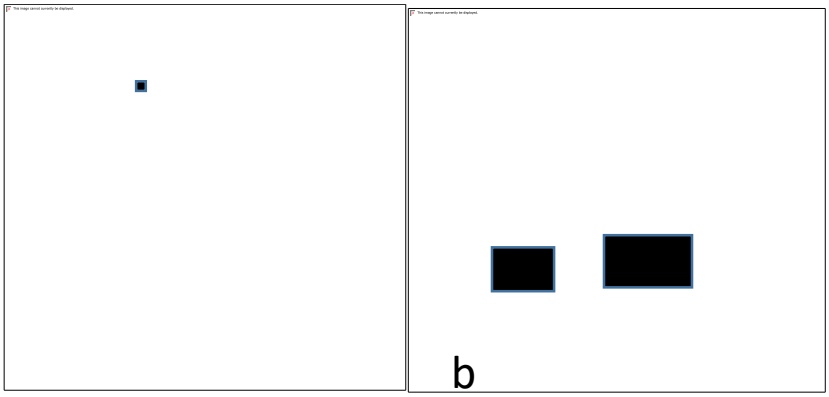


Fig 10 (a) showing patient position in 30 degree head end elevation and figure (b) showing a sunken flap

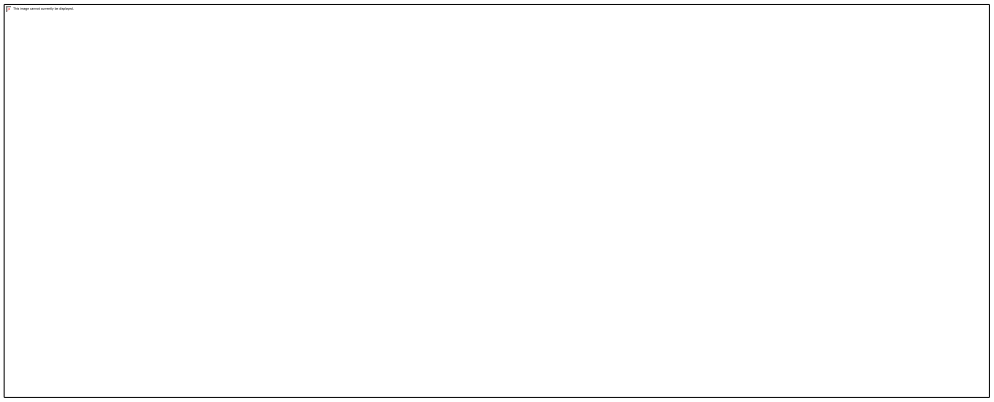


Fig 11 showing ONSD values in the left eye (a) and right eye (b) respectively

Head end 30 degrees down position

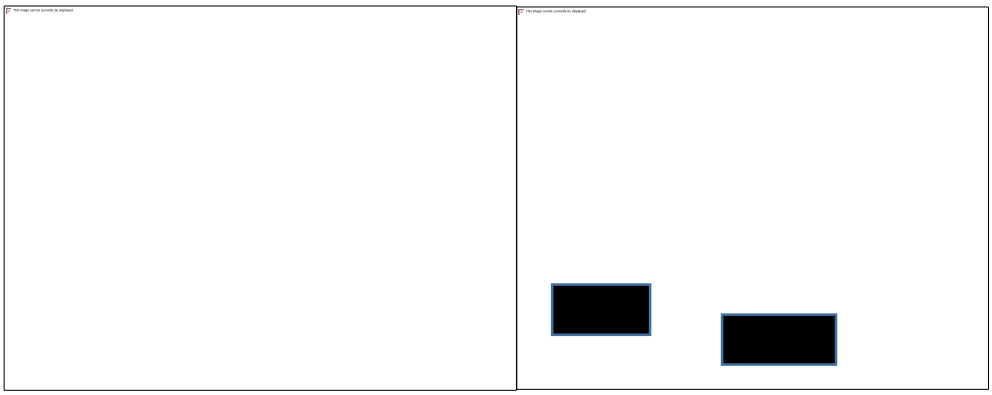


Fig 12 (a) showing patient position in 30 degree head end down and figure (b) showing full flap

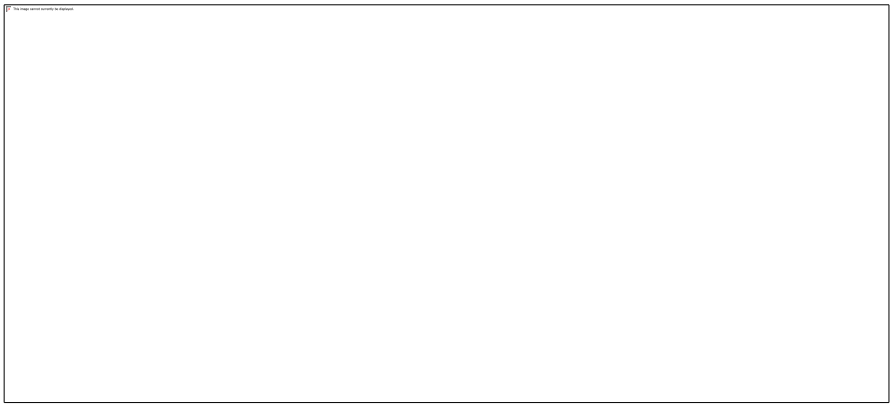


Fig 13 showing ONSD values in the left eye (a) and right eye (b) respectively

Post-operative measurement of ONSD

Head end 0 degrees

Figure 14 (a) showing post-operative measurement of ONSD with 0 degree head end elevation. Ultrasound images showing ONSD values in the left eye (b) and right eye (c) respectively

Head end 30 degrees elevation

Figure 15 (a) showing post-operative measurement of ONSD with 30-degree head end elevation. Ultrasound images showing ONSD values in the left eye (b) and right eye (c) respectively**.**

Head end 30 degrees down

Fig 16 (a) showing post-operative measurement of ONSD with 30 degree head down position. Ultrasound images showing ONSD values in the left eye (b) and right eye (c) respectively**.**

Table 10. ONSD values of patient X in pre-operative and post-operative period in three different positions

	Left eye average ONSD in mm	Right eye average ONSD in mm
Pre op 0º	5.1	5.2
Pre-op 30º up	5.1	5.2
Pre-op 30º down	5.3	5.5
Post-op1 0º	5.1	5.3
Post op1 30º up	5.1	5.2
Post op1 30º down	5.3	5.1
Post op3 0º	5	5.1
Post op3 30º up	5	5.1
Post op 3 30º down	5.1	5.2

DISCUSSION

Basis of the study

Ultrasound measurement of the optic nerve sheath diameter (ONSD) is now considered a reasonable proxy for intracranial pressure (ICP), with the advantages that it is non-invasive, can be repeated frequently and does not require shifting of the patient out of the ICU. ONSD measured by different techniques like magnetic resonance imaging (MRI), computed tomography (CT) and ultrasound all give comparable values. Studies which have correlated ONSD with concomitant ICP measurements using invasive methods have shown a sensitivity of 88% and specificity of 93%. (47)

Patients who have undergone a decompressive craniectomy will have altered intracranial pressure dynamics due to the fact that the "closed box" described by Munro and Kellie has been opened. In addition to the normal determinants of ICP such as intracranial volumes of brain, CSF and blood, atmospheric pressure also acts on the cranial cavity with varying effects. In normal closed craniums the ICP usually decreases when the head end is elevated due to increased venous drainage from the head. However in patients with the syndrome of the trephined the deficits that occur with change of posture are attributed to compression of the brain by atmospheric pressure. The deficits are usually marked when the patient is upright and decrease when the patient is horizontal. We therefore decided to measure the ONSD (as an indicator of ICP) in patients with open cranial cavities, expecting to find increased pressure with elevation of the head end. We theorized that we would be able to demonstrate a reduction in the ONSD with head end elevation postoperatively, and intended to correlate the degree of change with the degree of clinical improvement. The largest

differences were expected from patients who clinically had symptoms suggestive of the syndrome of the trephined.

ONSD variation in normal subjects

We initially measured the ONSD in healthy volunteers to investigate the variation in diameter with position (Table 1), and analysed the results using the paired t-test. There was no change in the ONSD in all subjects on head end elevation (mean change 0.01mm, p=0.68). On lowering the head end there was a trend towards a significant rise (mean increase 0.06mm, p=0.06) (Table 2), as would be expected with the head in a dependent position. There was no significant difference in the ONSD values between the left eye and right eye in normal healthy subjects as had been reported earlier by Romagnuolo et al. (48)

Inter-observer reliability

The measurements in 10 patients were performed by the Principal Investigator and an experienced member of the faculty to check on the accuracy of the measurements (table 9). The intraclass correlation coefficient (ICC) was very high, indicating a good agreement between the two observers and suggesting that all the measurements in subsequent patients and in the controls were accurate.

ONSD measurements in patients

On clinical evaluation of the patients most (26) had sunken scalp flaps in the neutral position which could have indicated that the brain was being compressed by atmospheric pressure. In the other 3 patients the flap was full when horizontal but in only one patient did it remain full even after head elevation. There were no distinguishing clinical features in these three patients. There was no evidence of raised ICP by ONSD measurement in any patient in the neutral position.

When ONSD measurements were performed in patients with cranial defects we found that in no patient was there an increase in the ONSD on elevating the head end, not even in the two patients who had symptoms suggestive of the syndrome of the trephined. In fact the ONSD decreased by an average of 0.05 mm between the neutral and head elevated positions. In 3 patients there was no change in the ONSD on head elevation, but the scalp flap in these patients was sunken both in the neutral and head elevated positions. This was a surprising finding that negated the assumption on which this study was based. We had proposed that the atmospheric pressure would compress the brain on elevating the head end, which is the generally accepted explanation for the syndrome of the trephined.

When the head end was lowered from the neutral position the ONSD increased by an average of 0.08 mm. This total variation of ONSD of 0.13 mm between head up and head down positions was more than that seen in the normal subjects (0.07 mm), and we wondered whether the actual benefit following cranioplasty was stabilisation of the pressure dynamics leading to a more stable intracranial environment, rather than an absolute reduction in pressure. The maximum variation between positions was in a young female patient with a difference in ONSD of 0.65 mm. However she did not have any postural change in symptoms, and the two patients with the syndrome of the

trephined only had variations of 0.07 mm and 0.10 mm, both of which were less than the average variation for all patients.

The cranioplasty in all patients was uneventful. When the post-operative variation of ONSD between head elevated and head down positions was compared to the pre-operative variation there was a mean decrease in the variability with the average decrease in ONSD on head elevation being 0.02 mm and increase in the head down position being 0.07 mm. This was an overall variability of 0.09 mm when compared to the pre-operative 0.13 mm and seemed to support our hypothesis of decreased variability. The mean values of ONSD in various positions pre- and post-operatively are recorded in table 7. The change of variability in all 29 patients is demonstrated in figure 6, with the value on the left being the variation in ONSD between head up and head down positions pre-operatively.

On further analysis the picture was not as clear, as we found that the variability had decreased in 17 patients and had actually increased in 12 patients. This is demonstrated in figure 7 where the patients who had a decrease in variability are on the left and those with an increase on the right, and in table 8 in which the mean values of ONSD in these 2 groups are recorded. In 17 patients the variability decreased from 0.14 mm (head up 5.09 mm, head down 5.23 mm) to 0.07 mm (head up 5.14, head down 5.21). In the remaining 12 patients the variability increased from 0.11 mm (head up 4.88 mm, head down 4.99 mm) to 0.13 mm (head up 4.89, head down 5.02). Since all patients remained well or improved, it was not possible to correlate this difference in variability with any clinical findings.

The decrease in variability was most marked in the young female patient mentioned earlier, with the variability changing from 0.65 mm to 0.2 mm, a decrease of 0.45 mm. However since she was asymptomatic pre-operatively there was no way of clinically interpreting this change. The two

patients with the syndrome of the trephine improved, and they also showed contrasting changes in variability – in one patient the variability decreased by 0.02 mm and in the other it increased by 0.10 mm.

We noticed that the mean ONSD in the supine position was higher (5.105 mm) in the patients who showed a decrease in the variability than those that showed an increase (4.97 mm), but this difference was not significant ($p=0.33$).

In conclusion, we expected to find that the ICP in patients with large craniectomies would increase on elevation of the head end, as this is the generally accepted explanation for the syndrome of the trephined. However in all our patients (including the two with symptoms suggestive of the syndrome of the trephined) the ONSD actually decreased on elevation of the head end, just as it did for normal subjects. The exposure to atmospheric pressure therefore did not result in any increase in the ICP, and the open cranial cavity behaved just like a normal closed cranium. Our secondary hypothesis that the cranioplasty might stabilize the intracranial pressure dynamics was also disproved, with pressure variability increasing in some patients and decreasing in others.

LIMITATIONS

1) The number of patients recruited was only 29 and analysis with a larger number of patients might yield different results.
2) Most patients in our study were well pre-operatively and only two patients had history suggestive of the syndrome of the trephined. If we had more patients with major symptoms we might have been able to better correlate the effect of the change in variability with clinical improvement.

CONCLUSIONS

1) In normal subjects the optic nerve sheath diameter does not decrease on head end elevation, and the increase on lowering the head end falls short of significance.
2) Sinking of the craniectomy scalp flap in supine or in head end elevated position is not associated with raised ICP. Therefore it is not possible to attribute any improvement in clinical status after cranioplasty to a removal of the effect of atmospheric pressure and a decrease in ICP.
3) The effect of cranioplasty on intracranial pressure dynamics in our study is mixed and cannot explain any change in clinical status.

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ANNEXURES

Information sheet

Title of study: Optic nerve sheath diameter (ONSD) measurements in normal subjects in three different positions - A prospective observational cohort study

Studies had shown that the pressure inside your brain can be indirectly measured by measuring the thickness of your optic nerve (nerve which help you to see). It is also proved by studies that there are pressure variations inside your brain according to your head position. In our study we are trying to find out that these pressure variations occurring inside your brain can be correlated with your optic nerve thickness or not and is there any difference in the thickness in your optic nerve when you are lying in three different positions. In order to check these pressure measurements, we can perform an ultrasound of the optic nerve that helps you to see. A measurement of its diameter with an ultrasound scan of your eye can give an idea of the pressure in the skull. By checking this measurement in different positions – sitting, lying down and lying down for 30 minutes after lowering the head end, we would like to check if there are any changes in measurement of this diameter. This study may not directly benefit you.. The measurement will be performed in each eye in lying down position, sitting up position and after lying down for some time with the head end being lowered. No complications have been reported following performance of this measurement. You may have mild discomfort when you have to lie with head end lowered and when the ultrasound probe is placed and moved over your eye.

For any clarifications regarding this study, you may contact

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Informed consent form

Title of study: Optic nerve sheath diameter (ONSD) measurements in patients undergoing cranioplasty for cranial defects after decompressive craniectomy for traumatic brain injury – A prospective observational cohort study

I, ……., residing at …….. of ……..(CMCH No:) Have been informed of the nature of the above mentioned ultrasound study by Dr. ……

I have read and understood the contents of the information sheet regarding the study and it has been explained to me that my/my relative's participation in the same is entirely voluntary. The nature of the study has been explained to me in a language that I have understood. I understand that I/my relative can withdraw from the study at any stage. I had the opportunity to clarify any doubts regarding the study and appropriate clarifications were obtained regarding the procedure.

I understand that by agreeing for participation in this study, the results of the study may be presented/published in a scientific journal/scientific forum without any of my/my relative's identity being revealed.

I understand that the study will not have any direct bearing on my/my relative's treatment and the results of the same may not benefit me/my relative directly.

I agree for my/my relative's participation in this study.

Name of person giving consent:

Age of person giving consent:

Signature/thumb impression of person giving consent:

Name/Signature of doctor who has obtained consent:

Name/Signature of person signing as witness, in case thumb impression is obtained:

Date:

Information sheet Study group 2

Title of study: Optic nerve sheath diameter (ONSD) measurements in patients undergoing cranioplasty for cranial defects after decompressive craniectomy for traumatic brain injury – A prospective observational cohort study

You had undergone an operation to remove part of the bone in your skull so that the pressure inside the skull could be reduced at the time you met with an accident. After examining you over the past few months in the outpatient clinic, we feel that you may benefit from an operation to replace the bone in your skull to fill the defect therein. This operation is called cranioplasty. When you have a defect in the skull bone, there may be changes in the pressure within the head when you sit up versus when you lie down. This pressure change may cause you to have changes in the way your brain functions. In order to check these pressure measurements, we can perform an ultrasound of the nerve that helps you to see. A measurement of its diameter with an ultrasound scan of your eye can give an idea of the pressure in the skull. By checking this measurement in different positions – sitting, lying down and lying down for 30 minutes after lowering the head end, we would like to check if there are any changes in measurement of this diameter. This study may not directly benefit you and will have no influence on the operation that you are going to undergo. The measurement will be performed in each eye in lying down position, sitting up position and after lying down for some time with the head end being lowered. These measurements would be done on each eye separately before the operation, on the first, third and tenth day after the operation. No complications have been reported following performance of this measurement. You may have mild discomfort when you have to lie with head end lowered and when the ultrasound probe is placed and moved over your eye.

For any clarifications regarding this study, you may contact

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Informed consent form Study group 2

Title of study: Optic nerve sheath diameter (ONSD) measurements in patients undergoing cranioplasty for cranial defects after decompressive craniectomy for traumatic brain injury – A prospective observational cohort study

I, ……., residing at …….

…….. of ……..(CMCH No:)

have been informed of the nature of the above mentioned ultrasound study by Dr. ……

I have read and understood the contents of the information sheet regarding the study and it has been explained to me that my/my relative's participation in the same is entirely voluntary. The nature of the study has been explained to me in a language that I have understood. I understand that I/my relative can withdraw from the study at any stage. I had the opportunity to clarify any doubts regarding the study and appropriate clarifications were obtained regarding the procedure.

I understand that by agreeing for participation in this study, the results of the study may be presented/published in a scientific journal/scientific forum without any of my/my relative's identity being revealed.

I understand that the study will not have any direct bearing on my/my relative's treatment and the results of the same may not benefit me/my relative directly.

I agree for my/my relative's participation in this study.

Name of patient/person giving consent:

Signature/thumb impression of patient/person giving consent:

Name/Signature of doctor who has obtained consent:

Name/Signature of person signing as witness, in case thumb impression is obtained:

Date:

NAME	SIDE	supine	up	down	Lpre S	Lpre30 up	Lpre 30 d	Lpos	Lpo 30 up	Lpo30 D	Rpres	Rpre30up	Rpre30D	Rpos	Rpo30up	Rpo30D
Manoj Kumar	RIGHT	sunken	sunken	full	5.33333	5.3333333	5.53333	5.3333	5.33333	5.5	5.25	5.4	5.46667	5.3667	5.33333	5.5
Vijayakumar	LEFT	sunken	sunken	full	4.66667	4.4666667	4.7	4.5667	4.23333	4.833333	4.66667	4.2333	4.86667	4.5333	4.3	4.7667
Soumya	LEFT	sunken	sunken	full	4.56667	3.9	4.83333	4.3667	4.33333	4.5	4.33333	4.3	4.66667	4.6667	4.56667	4.8
Menaka	RIGHT	sunken	sunken	full	4.83333	4.9	4.93333	4.8	4.66667	4.733333	4.86667	4.8	4.83333	4.6	4.73333	4.7667
Suresh	LEFT	sunken	sunken	full	4.46667	4.4333333	4.7	4.4333	4.5	4.6	4.46667	4.4333	4.63333	4.5	4.5	4.4667
Syed	BIFRONTAL	sunken	sunken	full	4.73333	4.6333333	4.74333	4.8	4.83333	4.966667	4.66667	4.6333	4.66667	4.8667	4.86667	4.9333
Faizal	BIFRONTAL	sunken	sunken	full	4.93333	4.7666667	5.03333	4.9	4.76667	5	4.93333	4.9	5.3	4.9333	5.03333	5.1667
Mohana Kavitha	LEFT	sunken	sunken	full	4.9	4.8666667	5.1	4.9333	4.9	5.066667	5.03333	5	5.1	5.0333	5.03333	5.2333
Chitti Babu	LEFT	sunken	sunken	full	5.36667	5.0333333	5.16667	5.1667	5.03333	5.3	5.13333	5.1667	5.26667	5.2333	5.2	5.2667
Vinayakam	RIGHT	sunken	sunken	full	4.93333	4.7666667	5.03333	4.8667	4.86667	5.1	4.9	4.8667	5.03333	4.9667	4.96667	5.1667
Damodaran	LEFT	sunken	sunken	full	4.63333	4.6666667	4.73333	4.7333	4.73333	4.766667	4.83333	4.7667	4.63333	4.8333	4.8	4.6667
Mamata	LEFT	full	full	full	5.06667	5.1	5.26667	4.8667	4.96667	4.933333	4.9	5.0667	5.4	5.0333	5.03333	5.1
Kanniyappan	LEFT	sunken	sunken	full	4.73333	4.5666667	4.73333	4.6	4.63333	4.72	4.56667	4.5	4.56667	4.6	4.66667	4.4667
Rup kumar	LEFT	sunken	sunken	full	4.73333	4.8333333	5.06667	5.4333	5.03333	5.466667	4.8	5.2	5.16667	5.3667	5.36667	5.3667
Praveen Kumar	LEFT	full	sunken	full	5.23667	5.2666667	5.03333	4.8667	4.83333	5	5.06667	4.8333	5.13333	4.9	4.96667	5.0667
Jeromiah	RIGHT	full	sunken	full	5	5.1666667	5.1	4.9667	5.23333	5.066667	4.93333	5.1	5.03333	5.0667	5.06667	5.1333
Jagathrachagan	LEFT	sunken	sunken	full	5.56667	5.6333333	5.56667	5.4667	5.3	5.333333	5.53333	5.6333	5.43333	5.2667	5.33333	5.4
Geeta	LEFT	sunken	sunken	full	5.76667	5.7333333	5.9	5.9	5.76667	5.8	5.76667	5.7333	5.73333	5.7333	5.8	5.8
Saravanan	RIGHT	sunken	sunken	sunken	6.06667	5.9666667	5.96667	5.7	5.73333	5.78	5.73333	5.5	5.26667	5.6667	5.36667	5.2667
Babu	BIFRONTAL	sunken	sunken	full	5.43333	5.4333333	5.53333	5.4667	5.43333	5.466667	5.33333	5.5667	5.56667	5.4333	5.46667	5.5667
Hayath Basha	RIGHT	sunken	sunken	full	5.56667	5.4333333	5.43333	5.4333	5.46667	5.566667	5.43333	5.3333	5.33333	5.4333	5.33333	5.4333
Ajith	LEFT	sunken	sunken	full	5.13333	5.1666667	5.26667	5.0667	4.93333	5.066667	5.26667	5.2667	5.3	5.1	5.1	5.0333
Kalairasan	RIGHT	sunken	sunken	full	5.26667	5.0666667	5.33333	5.2333	4.96667	5.066667	5.26667	5.1667	5.13333	4.9667	4.86667	4.8667
Saravanan	LEFT	sunken	sunken	full	4.9	4.7333333	4.86667	4.8667	4.83333	5	5.1	5.0333	5.03333	4.9	4.96667	5.0667
Thanjayan	LEFT	sunken	sunken	full	4.93333	4.8333333	5.13333	5.3333	5.33333	5.466667	5.03333	5.0333	5.16667	4.9667	5.1	5.2
Wakila Begum	LEFT	sunken	sunken	full	5.36667	5.2666667	5.26667	5.1333	5.03333	4.9	5.13333	5.1333	5.6	4.8667	4.9	5.0667
Punitha Kumar	LEFT	sunken	sunken	full	5	5.0333333	5	4.9	5.1	5.233333	5.13333	4.9333	5.06667	5.1333	5.26667	5.0667
Dinesh	RIGHT	sunken	sunken	sunken	4.76667	4.7666667	4.83333	5.5	5.73333	5.8	4.73333	4.7333	4.86667	5.6333	5.36667	5.2667
Pooja	LEFT	sunken	sunken	full	5.06667	5.0666667	5.16667	5.1333	5.13333	5.333333	5.13333	5.1667	5.2	5.1333	5.23333	5.1667